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IMMEDIATE MANAGEMENT OF THE INJURED URETER

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• *Serious injuries to the ureter have often resulted during trauma, such as stab and gunshot wounds, to the abdominal or pelvic organs, but they also occur occasionally during surgical procedures on neighboring structures, diagnostic procedures such as cystoscopy, and therapeutic procedures such as irradiation. Preoperative urographic study is important in planning the operative attack on certain abdominal, pelvic, and retroperitoneal spaces. Preoperative introduction of ureteral catheters should be utilized more frequently to facilitate identification of the ureters during difficult dissections. The unintended inclusion of a ureter in a ligature must be corrected promptly; the release of such a ligature is more readily accomplished by teamwork between the surgeon and the urologist. The possibility that a ureter has been injured should always be considered whenever oliguria or anuria is observed during the first eight hours after any surgical operation in the vicinity of the ureters. If evidence of injury or ligation is found, prompt repair, with provision for tissue drainage, is imperative.*

The ureter is frequently injured during surgical or urologic manipulative procedures. Gynecologic operations, such as hysterectomy, either vaginal or abdominal; the removal of the ovaries or fallopian tubes; excision of intraligamentous cysts or tumors; and vaginal repair for prolapse of the uterus, may be accompanied by ureteral injury. Operations on or within the abdomen, especially resections of the sigmoid and rectum; unusual conditions of the appendix, especially when retroperitoneal; the removal of atypical pancreatic and mesenteric cysts; and other less common procedures, are sometimes complicated by ureteral injury. Occasionally, a portion of the ureter, along with a segment of the bladder, is present in an inguinal hernial sac. In such a case, injury of the ureter may occur during surgical repair. In cystoscopic procedures, especially during ureteral manipulation of calculi, the ureter may be torn or perforated. Strictures of or kinks in the ureter, especially when long-standing ureteritis has been present, will present anatomic changes that predispose the ureter to injury by even the slightest trauma.

The most common ureteral injury brought about by the urologist is that due to perforation from the various instruments designed to facilitate the passage of ureteral calculi. Perforation of the ureter secondary to general body trauma is unusual. Injury due to external stab and gunshot wounds is seen in wartime but is uncommon in time of peace. After irradiation, the ureter may become necrotic and perforate into the surrounding tissues or into an adjacent viscus; but, more commonly, the wall becomes thickened and stenotic, and ureteral obstruction and hydronephrosis result. Ureteral injuries have become somewhat more frequent in recent years due to the increasing number of radical surgical procedures in the treatment of carcinoma of the lower part of the intestine, uterus, and pelvic adnexa. A marked increase in the number of injuries associated with cystoscopic procedures has been noted in the past 10 or 15 years.

The problems surrounding possible injury of the ureter are much more difficult and obviously more complicated for the abdominal surgeon and gynecologist than are those for the urologist. The latter is dealing directly with this structure and will be aware of the possibility of injury at all times. Failure to recognize the accident at the time of operation rules out the opportunity for immediate repair, and the most favorable time for repair of such ureteral damage is at the time of the mishap or as soon afterward as possible. The longer the situation exists unrecognized, the more difficult the anatomic correction and the more serious the complications.

Prevention of Ureteral Injury

Teamwork between the urologist and the gynecologist or abdominal surgeon will greatly lessen the number of surgical accidents to the ureter and bladder. While there is no single method that will insure prevention of these injuries—and it is obvious that they may be expected to occur even in the hands of the most experienced and capable physician—a preoperative knowledge of the anatomy and function of both kidneys and ureters is of great value to the surgeon.

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These can usually be demonstrated by a satisfactory excretion urographic study. If the information is incomplete, a retrograde study should be done. The careful surgeon will insist upon having these data before performing operative procedures that might be complicated by ureteral injuries.

Anomalies of the ureters and kidneys and possible distortions and deviations from their normal courses will be demonstrated by excretion or retrograde pyelograms. Renal fusion, renal ectopia, changes due to previous urinary infections, and the presence of cysts or tumors should be apparent before the surgical procedure. It is surely not too much to ask that an excretion urographic study be done prior to elective operative interventions of such magnitude that ureteral ligation or injury might result during a difficult dissection. So many lesions of the upper urinary tract are symptomless, or silent, that preoperative urograms should seem as important to the surgeon as do blood chemistry studies and other commonly applied laboratory procedures. Intestinal tumors occasionally involve the ureter by encirclement without localizing symptoms.

The urologist has, to a considerable degree, convinced the gynecologist and the abdominal surgeon of the value of use of the indwelling urethral catheter prior to and immediately after extensive operative procedures on the structures adjacent to the ureters and bladder. I urge the placing of indwelling ureteral catheters before the operation as well. Prior to the discovery of modern urinary antiseptics, there was some justification for feeling that the risk of setting up infection in the upper urinary tract might outweigh the help that the presence of these catheters might give in identifying the ureters more readily; however, this objection lacks validity today. It is true that the placing of catheters entails a cystoscopic procedure carried out by a well-trained person, who must see that the catheters are properly inserted and that they do not slip down during the operation. The latter can readily be effected by temporarily suturing the ureteral catheters to adhesive tape attached to the indwelling urethral catheter. It is true that occasions will occur where the ureters cannot be easily identified even with the catheters in place. However, in most of these instances the ureteral injury will become rapidly apparent by the appearance of the catheter during the course of the dissection. The objection that, by having catheters in place, the surgeon will be given a false sense of security against ureteral injury does not warrant serious consideration. I favor preoperative ureteral catheterization, and at Chicago Wesley Memorial Hospital there is an understanding that some member of the urologic service will be available for this purpose at all times.

Therefore, prevention of ureteral injury requires (1) recognition of the fact that such injuries can and will occur in the most experienced hands; (2) recognition that a knowledge of the relationship of the ureters to the abnormal structures that one is planning to remove should be obtained preoperatively by urography; and (3) recognition that the preoperative placing of ureteral and urethral catheters will assist the surgeon in avoiding a surgical accident to the ureter and bladder. The surgeon should be especially diligent in identifying the ureter (1) where it crosses the bifurcation of the iliac vessels; (2) in the ovarian fossae; and (3) where it passes behind the uterine artery. When the dissection is deep in the pelvis, he should at all times have in mind the location of the bladder wall and the intravesical portion of the ureter.

Most of the avoidable injuries to the ureter result from lack of vigilance in the placing of clamps and ligatures. Curiously enough, it seems that more ureteral and bladder injuries follow procedures where the dissection was reported as easy and satisfactory than where it was reported as difficult. In patients with extensive chronic inflammatory disease, large uterine or ovarian tumors, and infiltrating neoplasms of the colon, the surgeon will more often be accurately aware of the danger of ureteral injury and will go to greater pains in identifying the ureter in an early stage of the surgical dissection.

Treatment of Ureteral Injury

The immediate treatment of injury to the ureter (I am not taking into consideration delayed treatment) may be relatively simple or annoyingly complicated. When accidental ligation is recognized during operation, release of the ligation, with or without the passage of a ureteral catheter, will usually be adequate. If section of the ureter has occurred, one must accurately identify the proximal and distal segments and unite them, preferably over a catheter, by direct end-to-end anastomosis. Chromic absorbable surgical suture (0000) on an atraumatic needle is the suture of choice. Two or three mattress sutures suffice.

Since the immediate management of an injured ureter entails not only anatomic restoration but also insurance against urinary extravasation, the provision for adequate drainage, both intraureteral and alongside the ureter, must be of prime consideration. The introduction of a ureteral catheter by the cystoscopist while the surgeon is searching for or attempting repair of the severed ureter may be most helpful. Likewise, the point of catheter arrest in the case of ureteral ligation may quickly define the area to be examined by the operating surgeon. If the situation does not warrant prolonged search for the area of injury or if repair is too difficult or considered unsatisfactory, nephrostomy should be performed after the abdominal wound has been closed, with provision for adequate drainage. It is well known that complete, sudden, simple ligation of the ureter is usually followed by an asymptomatic renal atrophy preceded by a complete unilateral renal suppression. All too often the surgeon may be tempted to follow this easy path out of the difficulty of unilateral ureteral injury. However, this would be most unwise unless previous renal functional and urographic tests had demonstrated a normal kidney on the unaffected side. Even then one would recommend nephrostomy reluctantly, except in the unusual instance where later surgical procedures or complications might outweigh the loss of function of one kidney.

Releasing of ligation should always be seriously considered when complete anuria has been shown by cystoscopic examination to be due to bilateral ureteral occlusion. In the past, there has been a high mortality from this secondary operative procedure; and the sur-

geon has, therefore, preferred to perform a bilateral nephrostomy or pyelotomy. The release of a ligation can be greatly simplified if the surgeon and urologist cooperate in its performance. The surgeon reopens the laparotomy wound and, with the aid of the cystoscopist, can readily detect the points of constriction when the ureteral catheters (preferably 7 to 9 F. in size) are used to prod the area of obstruction. After release of a ligation, the catheters should be passed to the renal pelves and left in place for from 5 to 10 days. Without the help of the urologist, the surgeon may conduct a prolonged search for the areas of ligation, remove the wrong sutures, and generally grope in the edematous tissue without finding the offending ligatures.

In my experience, the most satisfactory manner of handling the problem of intraureteral drainage is to have the surgeon insert a 6 to 9 F. ureteral catheter, either woven, latex rubber or polyethylene, so that one end is in the renal pelvis and the other end coils up in the bladder. The latter end is then grasped with a forceps or cystoscopic rongeur and pulled out through the urethra. An indwelling urethral catheter should be placed in the bladder and the ureteral catheter fastened securely to it to prevent its slipping down the ureter into the bladder. If the ureter has been injured low in the pelvic portion, within 3 to 5 cm. of the bladder, reimplantation of the proximal portion to the bladder should be effected, using either the pull-through-and-suture technique or the eliptical anastomosis with mucosa-to-mucosa suture as described by Nesbit. When irreparable injury has occurred in the lower half of the ureter, one can either transplant it to the sigmoid or, if possible, effect a ureteroureterostomy. I have never performed the latter procedure, but it has been carried out successfully by Higgins, Parke Smith, and others.

Prevalence of Ureteral Injuries

Any patient who shows oliguria or complete anuria during the first eight hours after operation should be suspected of having ureteral injury or ligation, if the surgical procedure has involved the region of the ureters. In unilateral occlusion, there may often be no symptom whatever, but partial anuria, pain in the flank or abdomen, and elevated temperature may suggest the condition.

Ureteral injuries from perforation during the cystoscopic extraction of calculi from the lower part of the ureter have increased materially in recent years. Mechanical stone extractors are usually the instrument of injury. At the time of extraction, the ureter may be more vulnerable to puncture because of the inflammatory or necrotizing action of a long-impacted calculus. Ureteral injuries occurring as a result of cystoscopic procedures and those associated with external trauma, such as gunshot and stab wounds, make up a chapter too vast to consider here. Rusche and Hager have completed a comprehensive study of 103 ureteral injuries encountered by them during the years 1930 to 1950. The increase in ureteral injuries after cystoscopic attempts at ureteral stone extraction was emphasized, as were such injuries due to gunshot wounds. They felt that, despite the increase in the number of patients subjected to extensive radical pelvic and abdominal surgery, a comparison of the period 1940-1950 with the preceding decade indicated that the number of surgical injuries remained about the same.

Summary

The gynecologist, general surgeon, and urologist must constantly bear in mind the possibility of ureteral injury during operative procedures in the abdomen, pelvis, and retroperitoneal spaces. Preoperative excretion urographic studies are most important in considering the operative attack. Preoperative introduction of ureteral catheters should be utilized more frequently to assist the surgeon in more readily identifying the ureter. These catheters should be fastened to the indwelling urethral catheter. The release of a ligation is more readily accomplished by teamwork between the surgeon and urologist. Early surgical repair, with adequate provision for tissue drainage, is paramount after injury or ligation has been discovered.

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PRIMARY CARE OF THE URINARY TRACT IN SPINAL CORD INJURY

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The management of the bladder in patients with spinal injury or disease has two aims: to provide the patient with a micturitional function that will not impede his efforts toward rehabilitation and to preserve the integrity and function of the upper urinary tract. Fortunately, these aims are not incompatible; indeed, the best assurance of a healthy upper urinary tract is a normally functioning bladder. If this can be achieved and if, at the same time, the hazard of formation of renal calculi because of disturbed calcium

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• *The structural changes that follow retention of urine in a paralyzed bladder must be prevented by adequate drainage from the beginning. With a catheter in place, the bladder regains its ability to fill and empty by reflex action with a certain regularity. It can be conditioned by the method of tidal drainage within a period of 6 to 12 weeks. Meanwhile a program of high fluid intake, acidulation of the urine, and muscular exercise is carried out to prevent lithiasis. The catheter can then be removed, and the observance of a certain program of fluid intake and other habits enable many patients to maintain an adequate urinary capacity, to empty the bladder completely, and to get along without wearing any apparatus.*

metabolism can be obviated, the disastrous train of events that has in the past led so many of these patients to invalidism and death may be averted.

There are two principles upon which the course of management that meets these demands is based. First, any functional disturbance, such as that caused by impaired innervation, will eventually result in reciprocal structural alteration; furthermore, if the dysfunction leads to secondary consequences, such as infection, secondary changes will develop and may become so marked that, even if the innervation were to be restored, the end-organ might remain incapable of normal activity. The object, therefore, is to prevent the development of such changes, to recognize them if they have already developed when the patient is first seen, to evaluate their contribution to the dysfunction, and, finally, to treat them if possible. The other basic principle is that the bladder is a spinal reflex organ with an overlay of controls from higher centers. Primary neurogenic dysfunction may result from involvement of the spinal center itself or from interruption of the pathways through which it communicates with the brain.

To guard against structural alteration, one must insure adequate drainage from the beginning. Overdistention leads to changes in the bladder wall; these are hastened by infection, which soon develops. Even when the patient can void, if there is residual urine (which is often the case), infection will follow. Catheterization is not without its risks and inconveniences, but these add up to a good deal less than the danger of infection in an inadequately drained urinary tract. Furthermore, by preserving the structural integrity of the bladder, early drainage hastens the day when, the process of retraining having been completed, artificial drainage may be discontinued and the patient may void naturally through the urethra.

Having secured the advantages of early drainage, one may expect that, as the patient emerges from the period of spinal shock and as the reflex activity below the level of the lesion is resumed, the bladder, although deprived of its controls from higher centers, will fill and empty reflexly with some degree of rhythmical regularity. This is the so-called automatic bladder; but the term is a bad one, and the function represented is not satisfactory. Such a bladder tends to be hypertonic; its emptying contractions are inefficient, and, as a result, it accumulates a considerable amount of residual urine. There is, of course, no control of micturition. In the name of expediency, treatment has often taken the form of permanent suprapubic drainage, permanent urethral catheterization, or the wearing of some cumbersome type of incontinence apparatus. Most of these undesirable eventualities can be avoided.

The Reflex Bladder

Management is based upon the fact that reflex activity of any kind can be conditioned to greater consistency and efficiency. Tidal drainage provides a method of applying this conditioning process and achieving that degree of consistency and efficiency that is the primary requisite of good function. If the patient is seen early, before any complicating factors have developed, this can be accomplished in an amazingly short time, perhaps as little as six weeks. It should seldom require more than three months. The catheter may then be removed and, by combining a controlled fluid intake with careful habit training, the patient may maintain an adequate capacity, empty his bladder completely, and have reasonably good control, so that it is unnecessary for him to wear any apparatus. It should be possible to achieve and maintain such a result in at least two-thirds of all patients. The program for prevention of calculi is simple but effective. It includes a high fluid intake (3,500 to 4,000 cc. daily), acidulation of the urine, muscular activity to avoid the mobilization of calcium from the skeleton, and adequate drainage. On such a regimen, the incidence of primary renal calculus should be less than 2%. The weeks immediately after injury are most critical.

This is not the time to discuss the exact techniques employed in the routine urologic care of these patients, such as the conditioning of the reflex bladder, the details of habit training, the indications for nerve blocks or nerve interruptions in special cases—and I should like to emphasize that these seem to me to be indicated only in special cases—and the indications for and technique of transurethral resection, which, in my experience, has been necessary in perhaps one out of every four patients. It should be remembered that there is no place for mere expediency in the attack on this problem. Nothing but the best will do if the two aims mentioned earlier are to be achieved. If they are not, the patient cannot anticipate a successful rehabilitation and probably will not live very long; he will certainly not enjoy good health.

Comment

It is only fair to point out, however, that this method of treatment is not easy to follow. It requires meticulous daily attention to detail and seemingly endless explanations to patients, nurses, attendants and, in particular, to other doctors who are concerned in the patient's care. Above all, it demands the understanding and the willing cooperation of the patient, particularly during the difficult weeks of habit training shortly after the removal of the catheter. There is no way of avoiding this if the best results are to be obtained; I am not aware of any short cuts. The various surgical procedures that have at one time or another been suggested (some of which still have a useful place) are not substitutes for the fundamental program of conditioning of the reflex bladder but rather are supplements to it, to be employed when and if they are required, according to the needs of the individual patient. The other expedients to which I have referred briefly are easier for the doctor and make fewer demands upon the patient's understanding and cooperation. The only thing to be said for the more difficult approach recommended here is that it gives the majority of patients a much healthier urinary tract and keeps them alive and well longer.

NEUROSURGICAL ASPECTS OF TREATMENT FOR PATIENTS WITH SPINAL CORD INJURIES

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• *The first decision for the neurosurgeon after an injury to the spinal cord is whether any immediate neurosurgical maneuver is indicated. Neurological and roentgenographic examination determine whether fracture-dislocations need to be reduced, whether traction or laminectomy are necessary, and whether post-traumatic fragments of bone, intraspinal hematomas, or herniated intervertebral disks require attention. In many cases early laminectomy is actually the conservative course of action. Later problems for the neurosurgeon, from three months to several years after the injury, concern especially the intractable pain and spasticity that generally accompany paraplegia. Various procedures, including chordotomy, offer reasonable hope of relief of pain; alleviation of spasticity may be afforded by peripheral neurectomy, subarachnoid alcohol block, rhizotomy, or subtotal spinal chordectomy.*

Since I shall discuss only the aspects of the care of patients with spinal cord injuries that are directly related to neurosurgical management, it will be necessary to integrate these remarks with those of the other speakers on the panel (this issue, pages 1203-1204 and 1208-1209) in order to arrive at an over-all picture of management for patients with spinal cord injuries. As Dr. Covalt has stressed, the patient with spinal cord injuries should be taken directly to the x-ray department so that roentgenograms might be obtained without any additional moving of the patient. It is at this point, while the patient is still in the x-ray department, that a decision should be made as to whether neurosurgical care is immediately indicated, assuming that the neurosurgical consultant has been called to see the patient. After a detailed neurological examination and appraisal of the roentgenograms, the first decision that the neurosurgeon is called upon to make is whether any immediate neurosurgical maneuver is indicated.

Early Neurosurgical Treatment

In cases of fracture-dislocation of the cervical spine in which reduction must be carried out, this is usually performed properly by skeletal traction applied to the skull. The method that is commonly used is the application of Crutchfield tongs to the crown of the skull or wires passed through trephine openings in the skull. Thus, in a great majority of cases of fracture-dislocation of the cervical spine, proper reduction with decompression of the spinal cord, which is the initial treatment of choice, can be accomplished by skull traction. In cases in which skeletal traction properly applied has not been able to reduce the dislocation or in which a subarachnoid block persists despite adequate use of traction, cervical laminectomy with decompression is indicated. Another indication for open operation is progressive increase in neurological deficit despite satisfactory skeletal traction. In some instances of violent injury to the cervical portion of the spinal cord, acute herniation of the intervertebral disk also occurs. Usually, clinical and roentgenographic studies will aid in the diagnosis of this lesion, although occasionally myelography is necessary. In such instances, laminectomy with decompression of the spinal cord should be performed.

In cases of thoracic and lumbar fracture-dislocation, the subject of laminectomy versus more conservative management continues to be controversial, although an increasing number of neurosurgeons now seem to feel that laminectomy and decompression is the treatment of choice in almost every case. It has been my own policy to recommend that laminectomy be performed early in every case of paraplegia that is caused by injury of the thoracic and lumbar spine. It is my opinion that early, routine laminectomy in such cases is actually the conservative course of action and that it can be done safely and without causing any delay in the ultimate rehabilitation of the patient.

There are many reasons why laminectomy should be performed, some of which have already been enumerated in early reports. Very briefly, some of the reasons for laminectomy are as follows: 1. In the thoracic and lumbar region it is an operation that can be performed quickly, under local anesthesia if necessary, without interfering with the stability of the spinal column and with a mortality rate that is practically nil. 2. There is no way during the immediate post-traumatic period in patients demonstrating complete paraplegia to ascertain, by either neurological examination or roentgenographic examination, whether there has been an anatomic transection of the spinal cord. An examiner is not justified by either clinical examination or roentgenologic examination in concluding that the spinal cord has been irreparably damaged. The only way one can determine early, in patients demonstrating complete loss of motor and sensory function, whether the spinal cord is anatomically transected is by direct exploration. Therefore, the patient should not be denied laminectomy because the examiner has the impression that the spinal cord is already hopelessly injured. 3. It can be considered that in some cases the removal of depressed laminas and other post-traumatic fragments of bone as well as intraspinal hematomas may have a beneficial effect upon future spinal cord function. 4. Wide débridement with intradural exploration may help to prevent late arachnoiditis and other later complications, such as pain and spasticity. 5. If wide decompression of the injured area of the spinal cord is performed shortly after injury, early mobilization and rehabilita-

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tion may be instituted more safely than if the patient still has spinal cord compression. 6. Paraplegic patients logically conclude that direct exploration and decompression of the spinal cord should be attempted, if there is not some definite medical contraindication, before they are asked to resign themselves to a lifetime of paraplegia and a long period of rehabilitation for their paralyzed extremities.

Alleviation of Sequelae

During the late phases of care for the patient with spinal cord injuries, that is, from three months to several years after injury, the neurosurgeon may be able to play a role in alleviating some of the undesirable sequelae of paraplegia. For the purpose of this discussion, I shall limit myself to two of the most intractable and distressing complications of spinal cord injury, pain and spasticity. Although these phenomena are not both invariably present in the same patient, there is some justification for considering pain and spasticity simultaneously. Both of these phenomena are paradoxical neurological sequelae of spinal cord injury. In the case of pain, this sensation is usually referred to areas rendered anesthetic and analgesic by the spinal cord lesion, so that heightened pain sensation is present in an area from which the application of painful stimuli cannot be appreciated. Likewise, spasticity in patients with paraplegia reflects exaggerated involuntary motion of muscles that cannot be moved voluntarily. Thus, these phenomena, namely, pain referred to analgesic areas and exaggerated activity in paralyzed muscles, are considered to be physiologically related. Moreover, in evaluating the etiology of these distressing sequelae, there is considerable evidence that not only the destructive elements of traumatic lesions but also the irritative effects of such injuries must be taken into account. For these reasons, pain and spasticity may be considered together.

Management of Pain.—Approximately 75% of the patients who incur spinal cord injury will, at some time during their course, complain of some type of severe pain. Because of the nature of such an injury, which may render a large part of the body numb, pain in these patients is particularly difficult to evaluate. No single classification of pain in paraplegic patients has been suggested that can be considered inclusive. Moreover, an etiological classification is not feasible at this time, inasmuch as the individual roles of the sympathetic nervous system, spinothalamic tract systems, and unrelated pathways have not yet been elucidated in these cases. Since there are some obvious differences in the mechanisms productive of pain during the early weeks after injury and those productive of pain after this period, it is well to consider pain early and late after spinal cord trauma.

Early Pain: A surprisingly small percentage of patients complain of severe pain over the site of vertebral injury. Many vertebral fracture-dislocations are unattended by local pain. In my experience, local discomfort is more common in cases of cervical fracture-dislocation than in fractures in other regions of the vertebral column. The treatment dictated by consideration of spinal cord lesion, as outlined earlier (that is, early skeletal traction in cases of cervical lesions and early laminectomy in cases of thoracic or lumbosacral lesions), will invariably alleviate the pain produced by the bony abnormality. In the cases in which spinal fusion is indicated, this procedure will also lessen the likelihood of prolonged local pain. Consequently, local pain over the site of vertebral fracture seldom becomes intractable and is usually managed without difficulty.

The two common neurological causes of pain in the nerve root are cartilaginous compression and complete intraspinal subarachnoid block. The presence of a complete subarachnoid block, particularly in the lower thoracic or lumbar region, will often produce severe pain in both lower extremities. This pain is often sharp and lancinating in character, as well as constant and excruciating. It may be diffuse throughout the extremities. It is sometimes accompanied by burning paresthesias. The pain is aggravated by extension of the back, coughing, sneezing, or other activities that tend to increase intra-abdominal and thus intraspinal pressure. Roentgenologic examination may provide evidence of narrowing of the intraspinal canal, and the presence of a subarachnoid block is confirmed by spinal puncture with careful manometric studies. Once this block is demonstrated, early laminectomy with decompression of the block is indicated. Surgical decompression will usually result in prompt relief of pain due to this cause. Since the presence of an intraspinal block is in itself indication for laminectomy, further discussion of pain due to such a cause is not necessary.

Pain due to compression of one or more nerve roots even in the absence of an intraspinal block is not infrequent in cases of vertebral fracture-dislocation. Compression of such roots may be due to anterior dislocation of a fractured lamina, posterior dislocation of part or all of the body of a fractured vertebra, protrusion of bony fragments into an intervertebral foramen, or traumatic protrusion of an intervertebral disk. The occurrence of the latter phenomenon is more common than had formerly been thought and has been emphasized recently, particularly as a cause of neurological damage in the cervical region.

Radicular pain due to one of the afore-mentioned causes of nerve root compression is recognized by those qualities peculiar to root pain: 1. The pain follows the anatomic distribution of one or more nerve roots. 2. Paresthesias along the same distribution are not uncommon, particularly in cases of incomplete transection of the spinal cord. 3. The pain is aggravated by coughing, sneezing, or straining. 4. The pain is usually intensified at night after the patient has been in an extended or hyperextended posture for some time. 5. The pain is usually sharp and lancinating in character.

Careful neurological evaluation and roentgenologic study will usually indicate the site at which radicular compression is occurring. Roentgenographic demonstration of a fracture extending through one of the intervertebral foramens, an extreme narrowing of an intervertebral disk space, or an obvious bony abnor-

mality may indicate the vertebral site of nerve root compression. In some instances, in the absence of such roentgenologic findings and in the absence of a subarachnoid block, contrast myelography may be utilized as an adjunctive aid in evaluating the site and cause of nerve root compression following spinal injury. However, this latter procedure is to be avoided in such cases whenever possible. Many spinal cord injuries are accompanied by subarachnoid or intramedullary hemorrhages, arachnoidal lacerations, and other types of lesions conducive to fibroblastic reaction. Superimposed upon such a nidus, the introduction of iodized oil (Lipiodol) or iophendylate (Pantopaque) may contribute to the development of an adhesive arachnoiditis. This is a common finding in cases in which exploration is done one or more years after injury, and such arachnoiditis is undoubtedly a contributing factor in production of the sequelae of spinal cord trauma.

Surgical exploration and decompression is the treatment of choice in cases of pain due to nerve root compression. Hemilaminectomy, foraminotomy, or removal of a protruded intervertebral disk, depending upon whichever proves to be indicated, will often relieve radicular pain. Treatment of this type of injury to the spinal cord or cauda equina will be more successful in those cases in which decompression is carried out early, before the pain has become constant and before the patient has become dependent on narcotics.

One other cause of pain in paraplegic patients during the early days following spinal cord injury is the presence of concomitant injuries to other body parts, such as a ruptured spleen or traumatic hemothorax. Such a category is too obvious to require further elaboration and is mentioned only for the sake of completeness. However, I have seen patients in whom extraspinal injuries had been overlooked because of the initial examiner's preoccupation with the major symptom of paraplegia. Vigilance in a complete physical examination obviates such errors.

Late Pain: Pain of an intractable nature is more often a complaint of the patient three or more months after injury than during the early post-traumatic period. This pain has been classified by several authors. Most writers seem agreed that pain in the lower extremities may be of an intermittent, sharp, lancinating, radicular quality; a diffuse, dull aching quality; or a burning causalgia-like quality. The first type is most frequently seen in cases of injury to the cauda equina, while the second type is more commonly encountered in injuries of the spinal cord proper. The diffuse burning type of pain may be present in cases of injury to either the spinal cord or the cauda equina. Although the burning pain complained of by persons with paraplegia is similar to that usually described as causalgic, this type of pain in paraplegic patients is seldom, if ever, entirely relieved by sympathectomy. Holmes postulated that such persistent burning pain might be due to changes in the anterolateral columns of the spinal cord. Förster's investigations demonstrating that the entire pain pathway in the spinal cord is excitable substantiated Holmes' hypothesis. This still offers the best physiological explanation for the presence of diffuse aching, burning, tingling, or other nonradicular pains of the insensitive lower extremities of the paraplegic patient.

It has been my experience that all the categories of pain described in the preceding paragraph (that is, the radicular type of lancinating pains; diffuse, deep aching pain; or constant burning, tingling pains occurring in the insensitive paralyzed lower extremities), present three months or later after spinal cord injury, are best treated by bilateral high thoracic or cervical spinothalamic chordotomy. Like most neurosurgeons, I have had disappointing results with the use of spinothalamic chordotomy for pain in some paraplegic patients. However, if patients are selected who have not yet become addicted to narcotics and whose pain is not psychologically motivated, and if such patients are operated on under local anesthesia to allow instant appraisal of the level of analgesia achieved, the incidence of successful relief of pain will be reasonably satisfactory.

Relief of Spasticity.—In persons with traumatic paraplegia, spasticity of the paralyzed lower extremities becomes marked enough to impede rehabilitative measures in approximately 40% of those with injuries to the cervical and thoracic portions of the spinal cord. The relief of this spasticity will often enable a bedridden paraplegic patient to become ambulatory and self-sufficient. The four types of neurosurgical procedures that will alleviate intractable spasticity in the paraplegic patient are as follows: (1) peripheral neurectomy, (2) subarachnoid alcohol block, (3) rhizotomy, and (4) subtotal spinal chordectomy.

Peripheral Neurectomy: The resection of peripheral nerves has rather limited usefulness in relief of spasticity in paraplegic patients. It is confined largely to resection of the obturator nerves for relief of adductor, or scissors, spasticity. When the incapacitating spasticity is largely confined to the adductor muscles of the thighs, the procedure of choice is bilateral transabdominal obturator neurectomy. This procedure can be performed easily and provides immediate relief. The nerve is approached retroperitoneally through a McBurney abdominal incision and is readily identified as it emerges from the medial side of the psoas muscle to cross the brim of the pelvis. Stimulation of the nerve to produce adduction of the thighs positively identifies it prior to resection.

Subarachnoid Alcohol Block: Subarachnoid alcohol block has emerged as the single most useful and most applicable method available for relief of paraplegic spasticity. The indications for subarachnoid alcohol injection are essentially those previously applied to anterior rhizotomy. The chief indication is intractable spasticity of the lower extremities, which have no useful motor or sensory function. Enough time should have elapsed from the time of injury so that the lesion may be known to be stationary; this eliminates the possibility of future neurological recovery. This procedure has certain advantages over anterior rhizotomy: it is safer and more easily performed and is free of the hazards of major surgical procedure. Its effects are immediate and, in most instances, of long duration. It is, however, not selective. Thus, if certain

nerve roots, such as those to the detrusor urinae, are to be excluded, this method is contraindicated in favor of selective anterior rhizotomy. Such contraindications, however, are rare, particularly since it has been demonstrated that satisfactory autonomic micturition and sexual potency in the male can develop after subarachnoid alcohol injection.

The technique of subarachnoid injection I now use is as follows: The patient is placed on his side in bed, and the foot of the bed is elevated 18 in. An 18-gauge spinal puncture needle is inserted at the first lumbar interspace. A syringe containing 15 cc. of dehydrated alcohol is attached to the needle, and the alcohol is injected at the rate of 1 cc. every 15 seconds. An assistant constantly checks the patient's vital signs and the level of anesthesia during the injection. The injection is continued until both legs have become completely flaccid or until 15 cc. of alcohol has been injected. The patient is then turned on his back and kept in this position for four to six hours. He is allowed out of bed on the following day. If the injection has not produced satisfactory flaccidity, it is repeated the following day, with an additional 10 cc. of alcohol being used.

Rhizotomy: Rhizotomy, or intraspinal resection of nerve roots, is the time-honored method of relieving paraplegic spasticity, used since the introduction by Förster of posterior root section for spastic paraplegia. The fact that posterior rhizotomy alone did not provide adequate relief of spasticity led Munro to develop the technique of anterior dorsolumbar rhizotomy. This method requires laminectomy and division of all anterior nerve roots from the 10th thoracic through the 1st or 2nd sacral. The last firm dentate ligament is usually regarded as indicating the level of the first lumbar nerve root, although this relation is not invariable. If one is anxious to avoid sacrificing the motor supply of the detrusor urinae (usually the second and third sacral roots), these roots can be positively identified by stimulating each sacral root individually and at the same time recording the intravesicular pressure. Unless one is desirous of sparing certain nerve roots, such as those which innervate the urinary bladder, or unless some sensation exists in the lower extremities, subarachnoid alcohol injection is probably to be preferred to anterior rhizotomy.

Subtotal Spinal Chordectomy: Occasionally one is faced with the problem of recurrent spasticity after subarachnoid alcohol injection. In these circumstances the operation of anterior rhizotomy is made very difficult by the dense adhesive arachnoiditis produced by the prior alcohol injection. This arachnoiditis usually makes positive identification of individual roots impossible. In such cases, one may resort to subtotal resection of the spinal cord. This subtotal chordectomy involves resection of the spinal cord and nerve roots below the level of the 9th or 10th thoracic segment. The operation requires a laminectomy extending from the 9th or 10th thoracic to the first lumbar level and is performed more quickly and easily than is anterior dorsolumbar rhizotomy. McCarty has demonstrated that removal of the entire cord in man below the second thoracic level is not incompatible with life. In my experience, removal of that section of the spinal cord below the ninth thoracic level has had no untoward or unexpected sequelae.

Summary

During the early management of the patient with spinal cord injury, the neurosurgeon may contribute to the neurological evaluation. He may perform skeletal reduction of cervical fracture-dislocation and laminectomy as well as decompressive procedures when these are indicated. The principal sequelae that often require the attention of neurosurgeons during the later phase of this problem are intractable pain and spasticity. There are various neurosurgical methods that may be utilized in the management of these sequelae.

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REHABILITATION OF THE PARAPLEGIC PATIENT

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The rehabilitation of the paraplegic patient can only be accomplished with the closely knit cooperation of the neurosurgeon, urologist, orthopedic surgeon, and physiatrist. On admission, the patient should be taken directly to the x-ray room so that the neurosurgeon, having been called in to see him, can decide upon the advisability of surgery. The physiatrist should be called early to see the patient, who should be put on a Stryker frame or sponge-rubber mattress and turned every two hours. Particular attention should be paid to the skin over the sacrum and over the knees, as well as to that over the ischial tuberosities and the two trochanters. These areas should be cleansed carefully, massaged lightly, and oiled with some bland ointment or oil each time the patient is

• The end-result in rehabilitating the paraplegic patient is preparing him for a job, or at least preparing him for further vocational training that will result in a job. Total rehabilitation requires the cooperative services of the neurosurgeon, urologist, orthopedic surgeon, and physiatrist. The series of activities presented, which follow definitive care, are directed to the paraplegic patient's adjustment to walking and daily living.

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turned. It is important that the patient be placed in a neutral anatomic position, and, if necessary, splints should be put on to preserve the right angle of the foot on the ankle.

The physical therapist should be given instructions about exercising the joints of the patient's paralyzed extremities through a complete range of motion. Also, the patient should be given exercise for stretching the Achilles tendon. While the patient is in bed, either waiting for a laminectomy or recuperating from the operation, he should be given exercises to strengthen the muscles of the upper extremities. These are the muscles that will help him to walk after he is given braces. Particular attention should be paid to the triceps and latissimus dorsi muscles.

I do not recommend use of the triangular overhead bar, as some do, to aid patients in pulling themselves up into a sitting position; the patient only needs enough strength in the biceps to feed himself. Therefore, our patients are instructed to push themselves up with their hands placed behind them. This utilizes the triceps muscles and enables the patient to gain a sitting position. As soon as clearance is obtained from his neurosurgeon and/or orthopedic surgeon, the patient should be placed on a tilted board, with straps over his chest, hips, and knees, and should be allowed to stand in a vertical position. To start with, he should be allowed to stand at an angle of 25 to 30 degrees and only for a few minutes. This should be gradually increased, so that at the end of two weeks he should be standing in a vertical position for at least one hour a day. We know from research work that has been done [1] that an hour of standing a day will keep the calcium in the long bones of the legs and help to prevent urinary calculi and infection, which is the killer of paraplegic patients.

Braces should be ordered as soon as possible. We use as a rule of the thumb the 10th thoracic vertebra as a starting point. Those patients with lesions at T-10 and above are usually given double bar long braces with pelvic band and Knight spinal attachment for the back; those with lesions from T-10 to L-1 are given double bar long leg braces with pelvic band; and those with lesions below L-1, depending upon the musculature present, are given long leg braces.

Walking and Daily Living

The patient is brought to a standing position in the parallel bars and is usually started out with a "drag to" gait; he then advances to a "swing to" gait and, finally, a "swing through" gait. As soon as he is proficient in the parallel bars, the bars are eliminated and he is given crutches and taught to ambulate, at first with assistance and later by himself. The patient must be taught to climb curbs. We usually start with a 2-in. curb and graduate to a 4-in. curb and, finally, a 6-in. curb. Next, the patient must be taught to climb stairs. This is ordinarily taught with a one-hand rail and one crutch, the patient being allowed to carry the other crutch.

Also, the patient must be given an intensive course in activities of daily living. This would include training in transfer activities such as those from the bed to the wheelchair and back again, from the wheelchair to the toilet and back again, and from the wheelchair to a standing position and back again. He must be taught how to dress himself as well as all personal hygiene activities. Last, but not least, the patient must be taught to drive his own car, utilizing some of the simple hand-control devices that can be installed very inexpensively. Bowel and bladder training is most important. Bowel function is controlled by means of careful diet and the use of glycerin suppositories every other day. The majority of our patients do develop an automatic bladder control. However, since many of these patients return to active lives, they must be protected by some type of rubber urinal.

While the paraplegic patient is finishing his physical restoration, it is important that vocational possibilities be explored. In that way, when the patient is ready to leave the rehabilitation center he will know that he is prepared either to go to a job or to take further vocational training that will result in a job.

Summary

The patient with paraplegia should be kept on an active rehabilitation program from the time he is admitted to the hospital until he is discharged. He should be taught to become as self-sufficient as possible. Vocational possibilities should be explored, so that he may return to a job as soon as possible or may go on to further vocational training. Early rehabilitation procedures help to prevent the complications to which these patients are so liable. Later, the program must become more active and should include training in ambulation with braces, wheelchair activities, and hyperdevelopment of the patient's remaining muscles.

400 E. 34th St. (16).

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Capillary Thrombosis.—Capillary thrombosis is observed in a number of conditions. Extensive involvement has been reported in a variety of diseases, such as rickettsial infections, disseminated lupus erythematosus, periarteritis nodosa, malignancy, aplastic anemia, and thrombotic thrombocytopenic purpura. The pathogenesis is as yet undetermined. Moschcowitz was the first to report an instance of thrombotic thrombocytopenic purpura; this he did in 1925. He believed the thrombi consist of agglutinated erythrocytes, and pointed out that there is no evidence of primary vascular disease. Altschule ascribed the lesions to damage to the vascular endothelium, with secondary deposition of platelets. Muirhead and associates reported one case in which there were extensive endothelial proliferation, "platelet" thrombi and simultaneous "glomerulitis." Gore suggested that the earliest prethrombotic lesion in thrombotic thrombocytopenic purpura is a swelling of the subendothelial hyaline material, followed by rupture of the endothelium, with deposition of platelets on the injured spot and formation of a bimorphic thrombus. Endothelial proliferation and organization of the thrombus would then take place, only to be followed by new depositions of platelets, bringing about thrombocytopenia. Two of his five patients had a leukemoid blood reaction. In most cases reported, a shift to the left, with immaturity, was noted in smears of peripheral blood, but leukemia was ruled out. The clinical picture is rather typical, although not specific for the condition.—K. O. Husebye, M.D., J. M. Stickney, M.D., and W. A. Bennett, M.D., "Platelet" Thrombosis in Leukemia, *Annals of Internal Medicine*, May, 1956.

ABO BLOOD GROUPS AND DISEASE

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• *The existence of an association between certain diseases and the ABO blood groups was investigated by studying the blood-type frequencies of 158 patients with pernicious anemia, 908 with gastric carcinoma, 1,839 with peptic ulcer, 866 with carcinoma of the breast, 395 with carcinoma of the lungs, 256 with carcinoma of the colon and rectum, 456 with leukemia, 327 with congenital anomalies, and 184 with ulcerative colitis, and comparing them with the blood-type frequencies observed in blood donors. The strongest association found concerned peptic ulcer; statistically significant associations also were found for gastric carcinoma and pernicious anemia. Patients with pernicious anemia were distributed between groups A and O in the ratio 1:0.78, while the control patients exhibited the ratio 1:1.10. So great a difference in a sample of this size would have been found as an accident of sampling less than 5 times in 100, and is therefore accepted as significant. The incidence of gastric carcinoma was also greatest in persons with blood type A; that of peptic ulcer was greatest in persons with blood type O. The data suggested, but did not suffice to prove, an association of blood group with pulmonary and mammary carcinoma. No evidence was found of association with carcinoma of the colon and rectum, leukemia, ulcerative colitis, or congenital anomalies.*

Although the first half of the 20th century has seen the rapid expansion of the science of genetics, there has not been comparable growth in that branch concerned with human inheritance. This is related to a long gestation period, small family size, and a scarcity of characteristics inherited in a sufficiently simple manner to make practical a study of the genetic mechanisms involved. Undoubtedly, the impossibility of bringing about experimental mating in humans has played a major part. The blood groups, however, provide the specialist in human genetics with an almost ideal tool for use in his studies. Being all-or-none characteristics, they are readily classified, and their method of inheritance is exactly known. A practical illustration of the latter is their use in paternity problems. That considerable thought has been given to the possibility of an association between the ABO blood groups and disease is indicated by the numerous reports since 1920. Most of the early studies were done elsewhere than the United States. The results of these investigations were conflicting and inconclusive. At the time of the comprehensive review by Lessa and Alarcao[1] in 1949, there still was no convincing evidence of such an association, although Levine, Katzin, and Burnham[2] in 1941 had demonstrated the role of rhesus blood types in erythroblastosis fetalis.

In 1951, Struthers[3] found that, in Scotland, there was an increased (higher than expected) frequency of blood type A among children dying of bronchopneumonia during the first two years of life. Widespread interest was kindled among geneticists, immunologists, general biologists, and clinicians by the report of Aird, Bentall, and Fraser Roberts[4] in 1953 indicating a highly significant increased frequency of blood type A and decreased (lower than expected) frequency of blood type O among 3,632 patients with gastric cancer in England and Scotland; similar findings were subsequently reported by Hollander[5] from Switzerland, Køster, Sindrup, and Seele[6] from Denmark, and our group[7] from the United States. In 1954, Aird and co-workers[8] reported data indicating an even more highly significant association with peptic ulcer characterized by an increase in O and decreases of the other blood-type frequencies in 3,011 patients. These findings were confirmed by Clarke and associates[9] in Great Britain, Køster, Sindrup, and Seele[6] in Denmark, and our group[10] in the United States. However, our results indicated no significant difference between duodenal and gastric ulcer, whereas the other investigators obtained dissimilar findings for the two; gastric ulcer did not show the highly significant increase in type O and decrease in type A noted for duodenal ulcer.[8] McConnell, Pyke, and Fraser Roberts[11] have found a significant increase in frequency of blood type A in male patients with diabetes mellitus in England, which they feel merits only a tentative conclusion of an association; there was no evidence of a similar association in women. Likewise, there does not appear to be an association to age of the patients, as was earlier suggested.

The failure of earlier studies to demonstrate the existence of the now-noted associations may be explained by the small size of the series, absence of disease specificity with regard to patient groups studied, unsatisfactory controls, and the failure to use proper methods of statistical analysis. However, since these considerations have been appreciated, in addition to the positive findings discussed above, the results of other, negative investigations have been reported. From England, in 1954, Aird and others[8] reported no association for carcinoma of the colon and rectum (2,599 cases), breast (1,017 cases), and bronchus (998 cases); McConnell, Clarke, and Downton,[12] in 1954, reported none for 777 cases of carcinoma of the lung. The initial evidence of an association of the ABO blood groups to toxemia of pregnancy has not been supported by later data collected by the same authors and Dickins and co-workers.[13] In 300

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cases of gynecologic cancer, Krokfors and Kinnunen [14] in Finland in 1954 were unable to find evidence of an association. Maxwell and Maxwell [15] in 1955 reported their findings indicating no association in 2,147 patients with essential hypertension in Scotland.

This report is concerned with the results of the investigations of the ABO blood-type frequencies in patients with several diseases at the State University of Iowa Hospitals. The authors of previous investigations done in the United States concluded there was no evidence for an association of the ABO blood groups and the diseases studied; these investigations are discussed in other communications.[16]

Clinical Material and Procedure

The case material was provided by patients seen at the University Hospitals, except for some of the cases of gastric carcinoma, peptic ulcer, and breast carcinoma, as will be indicated. To insure the high degree of homogeneity with regard to categories of disease vital to this study, only patients with ironclad diagnoses were included. Microscopic proof was required for the carcinomas, while unequivocal clinical findings were regarded as mandatory for other diseases. In addition to the diagnostic criteria, the only other factor acting to select cases was information concerning the patient's blood type. The case records of all patients with the various diagnoses made available by the record room files were reviewed and included if satisfying the two forementioned requirements. To eliminate possible errors resulting from collection by multiple investigators, we selected and recorded all the data. Innumerable statistical studies were made feasible by transferring the collected data to punch cards and then using machine methods for tabulation and sorting.

The procedure employed in analyzing the data was to compare the blood-type frequencies noted in groups of patients with those observed in a normal population sample. Healthy blood donors who were friends and relatives of the patients and who came from the same geographical area and had similar ethnological and anthropological origins were used. In table 1 are recorded the data collected by tabulating the blood types of consecutive blood donors at a Des Moines and the University Hospital blood bank. In column C are the combined data, which were used as controls for comparison with the blood-type frequencies noted in the patients. Note the close agreement of the blood-type frequencies of University Hospital patients receiving consecutive transfusions, excluding only those with diagnoses of peptic ulceration or malignancy, with those of the blood donors used as controls.

TABLE 1.—*Blood-Type Distribution in Groups Studied*

Blood Type	A University Hospitals Donors		B Des Moines Donors		C Controls*		D University Hospitals Patients†	
	No.	%	No.	%	No.	%	No.	%
O	2,149	45.8	743	45.8	2,892	45.8	1,134	45.8
A	1,953	41.7	672	41.4	2,625	41.6	1,030	40.8
B	423	9.0	147	9.1	570	9.0	246	10.0
AB	165	3.5	61	3.7	226	3.6	84	3.4
Total	4,690	100.0	1,623	100.0	6,313	100.0	2,454	100.0

* Combined data (col. A and B).
† Patients with peptic ulcers or neoplasms excluded.

TABLE 2.—*Blood Types in Controls and in Patients with Pernicious Anemia*

	Type				
	O	A	B	AB	Total
Pernicious anemia	59	76	14	9	158
Controls	2,892	2,625	570	226	6,313
Totals	2,951	2,701	584	235	6,471

The statistical significance of differences noted between the patients' and the controls' blood-type frequencies was tested by the chi-square method, which naturally weights the disease to match the size of the control group. An additional test in the form of the method of difference in percentages based upon the normal curve theory has been applied to the data at hand. In a consideration of the various methods of examining these data, comparison of the differences in the frequencies of the four blood types between patients and controls is the obvious and perhaps first one that should be applied. For example, let us examine all of the blood-type findings in the patient and control groups for pernicious anemia at the 5% level of significance (table 2). In this case chi square equals 6.772 with 3 degrees of freedom. Since the value of chi square at the 5% level of significance with 3 degrees of freedom is 7.815, we have a result that is not regarded as significant at the 5% level. However, we observe that $0.05<p<0.10$, and so it might be worthwhile to conduct an additional study involving more data or to examine these data in greater detail.

Since in the instance of each disease studied, more than 85% of the patients had blood type O or A, and since the major differences from the controls most often occurred in O and A, it was believed desirable to examine the data as to the statistical significance of the reciprocal changes in frequencies of the O and A blood types. This afforded an opportunity to compare the results with those of other investigators who for the most part have used this method of analysis.

In particular, let us examine the frequencies with which types O and A occurred in the patients with pernicious anemia and compare them with the fre-

TABLE 3.—*Frequency of Types O and A in Patients with Pernicious Anemia and in Controls*

	O	A	Totals	Type A, %
Pernicious anemia	59	76	135	0.5630
Controls	2,892	2,625	5,517	0.4758
Totals	2,951	2,701	5,652	

TABLE 4.—*Blood Types in Patients with Gastric Carcinoma and Peptic Ulcer and in Controls*

	Blood Type							
	O		A		B		AB	
	No.	%	No.	%	No.	%	No.	%
Gastric carcinoma (208 cases)	88	42.2	116	55.8	84	9.2	25	2.8
Peptic ulcer (1,839 cases)	983	53.5	679	36.9	134	7.3	43	2.3
Controls (6,313 donors)	2,892	45.8	2,625	41.6	570	9.0	226	3.6

quencies in the controls. The following 2 × 2 contingency table (table 3) states that among this total of 5,652 persons there were 59 who had pernicious anemia and whose blood was of type O. Calculations based on the subtotals show that, if there were no association between blood type and pernicious anemia, 65 patients would be expected to show this

TABLE 3.—*Number of Patients with Carcinoma of the Breast by Blood Type and Hospital*

	Blood Type			
	O	A	B	AB
University Hospitals (371 cases)	244	253	56	18
Iowa Methodist Hospital (Des Moines) (126 cases)	57	63	9	9
Mercy Hospital (Iowa City) (157 cases)	69	67	16	5
Totals (654 cases)	370	383	81	32

combination simply by chance, for 2,701 × 135/5,652 = 65 (approximately). But the figure actually found, namely, 76, exceeds the expected number by 11. The following calculation of chi square for a fourfold table (which has 1 degree of freedom) shows that so great a discrepancy between the actual and the expected would occur by chance less than 5 times in 100:

$$X^2 = \frac{[(59)(2,625) - (76)(2,892)]^2 (5,652)}{(2,951)(2,701)(135)(5,517)} = 4.012$$

From tables of chi square it can be seen that a value of 4.012 corresponds to a value of p between 0.02 and 0.05, and it can be asserted, therefore, that the frequency of blood type A was significantly higher among the patients with pernicious anemia than among the controls.

Further consideration based upon the difference in percentages based upon the normal curve theory:

$$t = \frac{0.5630 - 0.4758}{\sqrt{\frac{(0.5630)(0.4370)}{135} + \frac{(0.4758)(0.5242)}{5,517}}} = \frac{0.0872}{0.0477} = 1.83$$

yields a value that is slightly lower than that at the 5% level. However, any test that reveals a significant difference should not be overlooked. Consequently, this study suggests that the frequency of blood type A is significantly higher in patients with pernicious anemia than in the controls. In addition to the two methods illustrated, other comparisons taken two and

TABLE 6.—*Blood Types of Patients with Carcinoma of the Breast*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	370	42.7	−3.1	2.861	0.05<p<0.10
A	383	44.2	+2.6		
B	81	9.4	+0.4	2.877	p>0.10
AB	32	3.7	+0.1		
Total	866	100.0	0.0		

three at a time (such as O and B or O and A and B) were made where indicated. Only the results of the first two comparisons will be reported.

Results

The findings for patients with gastric carcinoma and peptic ulcer are summarized in table 4. When the blood-type frequencies noted in the patient and control groups were compared, levels of significance for the observed differences were noted at 2% for gastric carcinoma and 0.1% for peptic ulcer. The detailed data and discussion concerned therewith are included in other articles.[10] In table 5 are recorded the data, collected from three hospitals, relative to carcinoma of the breast. No significant differences were found between the blood-type frequencies of the patients from the different hospitals. For purposes of the further statistical analysis, these data were combined. The results of the O-A and the O-A-B-AB comparisons are recorded in table 6. Of interest is the chi-square value for the O-A comparisons indicating a level of significance at 10%, as compared with the O-A-B-AB comparison, where there was no evidence of significance.

Patients with carcinoma of the lung were studied as one sample and were not subdivided by cell type. As will be noted in table 7, the O-A comparison was

TABLE 7.—*Blood Types of Patients with Carcinoma of the Lungs*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	202	51.1	+5.3	4.643	0.05<p<0.05
A	141	36.5	−5.1		
B	33	8.4	−0.6	5.220	p>0.10
AB	16	4.0	+0.4		
Total	395	100.0	0.0		

significant at the 5% level. That is, the observed discrepancy between the expected and the actual would arise by accidents of sampling 5 times in 100. That it did so arise seems the more likely when one notices that, in the examination of the entire group, the differences among the four types could have arisen by

TABLE 8.—*Blood Types of Patients with Carcinoma of the Colon and Rectum*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	119	46.5	+0.7	0.139	p>0.10
A	108	40.3	−1.8		
B	24	9.4	+0.4	0.293	p>0.10
AB	10	3.8	+0.2		
Total	256	100.0	0.0		

chance 10 times in 100 and are therefore not to be considered significant. This may be due to the fact that the slightly increased AB and decreased B frequencies in the patients as compared with the controls balanced one another. The data with regard to patients with carcinoma of the colon and rectum appear in table 8. No evidence of statistical significance was discovered when comparisons of the O-A or the O-A-B-AB differences were made. When colonic (153 cases) and rectal (103 cases) carcinoma were examined separately, likewise no evidence of an association to blood type was found.

Although most of the leukemias studied were either lymphatic or myeloid in type, small numbers of the less common ones were included. No evidence of an association to the ABO blood groups was found (table 9). The congenital anomalies studied have included those of the nervous, cardiovascular, respiratory, geni-

tourinary, and gastrointestinal systems. Inspection of the combined data recorded in table 10 indicates that no statistically significant differences were found. Study of each separate group failed equally to show evidence of statistically significant differences. No evidence was found to suggest an association between the ABO blood groups and ulcerative colitis. These data are recorded in table 11. Although relatively few cases were available for study, evidence suggesting an association to the ABO blood groups, as already illustrated, was found in patients with pernicious anemia. These data are recorded in table 12. It will be noted that the evidence was strongest when the O and A comparison was made.

Comment

In the evaluation of the results of this or any similar study, reliable controls have been regarded as most important. This reliability is determined by whether

TABLE 9.—*Blood Types of Patients with Leukemia*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	226	49.6	+3.8	1.732	p>0.10
A	179	39.3	−2.3		
B	40	8.7	−0.3	3.575	p>0.10
AB	11	2.4	−1.2		
Total	456	100.0	0.0		

or not the controls are truly representative of the population from which the patients came. For reasons stated in another article,[10] our controls would seem to compare favorably with those used by the other authors. The possible existence of unrecognized factors acting to select blood donors and thus altering the results

TABLE 10.—*Blood Types in Patients with Congenital Anomalies*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	136	47.7	+1.9	0.046	p>0.10
A	120	42.2	+0.8		
B	22	6.7	−2.3	2.147	p>0.10
AB	11	3.4	−0.2		
Total	327	100.0	0.0		

of the comparisons with control patients has been considered. Whether blood donors are satisfactory controls and whether the concept of normal population controls for these investigations is valid are two questions not finally answered, which are the subject for continuing study.

As mentioned before, rigorous diagnostic criteria must be insisted on in categorizing patients for study. Patients who could not be regarded as having ironclad diagnoses were rejected. Pernicious anemia presented a particularly good example of this point. Although more than 600 cases were noted in the record-room files, only 158 of these patients were judged to have ironclad diagnoses, with achlorhydria, macrocytic hyperchromic anemia, megaloblastic bone marrow, and proper response to therapy. Absence of information relative to blood type eliminated a substantial number of patients.

The findings in gastric carcinoma agree with those reported by Aird, Bentall, and Fraser Roberts,[4] Hollander,[5] and Køster, Sindrup, and Seele.[6] Similarly, with the exception of the previously indicated difference in regard to gastric ulcer, our findings in peptic ulcer are in accord with those reported by Aird and

TABLE 11.—*Blood Types in Patients with Ulcerative Colitis*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	80	43.5	−2.3	0.582	p>0.10
A	82	44.6	+3.0		
B	15	8.1	−0.9	0.773	p>0.10
AB	7	3.8	+0.2		
Total	184	100.0	0.0		

co-workers,[4] Clarke and associates,[5] and Køster, Sindrup, and Seele.[6] Aird and co-workers [4] found no significance in the differences of the blood-type frequencies between controls and patients with carcinoma of the breast. Our finding indicating an increase in type A frequency of a level of significance at 10% for the O and A comparison is not to be interpreted as conclusive evidence of an association between mammary carcinoma and the ABO blood groups. It will be interesting to observe the results of future studies of this kind.

A similar situation exists for lung carcinoma, for which Aird and associates [4] and McConnell, Clarke, and Downton [12] found no data of statistical significance. There is a need for study of more cases before proper interpretation at the 5% level of significance found for the O and A comparisons may be made. It is of interest that here, as in mammary carcinoma, comparison of the four blood-type frequencies rather than just O and A showed no statistically significant differences, the rather large differences in O and A frequencies being neutralized by absence of differences for types B and AB. In our series, 12.5% of 348 patients were Rh negative as compared with 15.7% of the controls; this difference is not statistically significant. There is an obvious need for collection of more data regarding this point.

The failure to find any evidence of significance for the differences observed in colonic and rectal carcinoma, leukemia, ulcerative colitis, and in patients with

TABLE 12.—*Blood Types of Patients with Pernicious Anemia*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	50	37.3	−8.5	4.012	0.02<p<0.05
A	76	48.1	+6.5		
B	14	8.9	−0.1	6.722	0.05<p<0.10
AB	9	5.7	+2.1		
Total	158	100.0	0.0		

congenital anomalies, although not excluding the possibility of an association between these diseases and the ABO blood groups, makes it seem unlikely. In view of the similar findings of Aird and others [4] for carcinoma of the colon and rectum, the possibility of such an association in these disorders seems most unlikely. The findings reported by Tinney and Watkins,[17] in

1941, support the absence of any statistical significance for the data concerning leukemia. We are unaware of other similar data pertaining to ulcerative colitis or congenital anomalies.

Because of the heretofore recognized relationship between gastric carcinoma and pernicious anemia,[18] it is of a particular interest to note that evidence exists of an association to the ABO blood groups characterized by an increase in type A and decrease in type O frequency. These findings are in accordance with those of Aird [19] and differ from those of Køster, Sindrup, and Seele.[6] The implications of the association of pernicious anemia, gastric cancer, and the ABO blood groups, in view of the evidence of the role of heredity in gastric cancer,[20] are interesting and merit further investigation.

The level of statistical significance for the differences in the blood-type frequencies between the groups of controls and patients is a function of the size of that difference and the number of patients available for study. This latter factor has played a major role in our investigations, the size of our series of patients being limited by the number of patients (1) satisfying the diagnostic criteria and (2) for whom blood-type information was available. In the instance of each disease studied, with the possible exception of duodenal ulcer, it would have been desirable to have had more cases. However, from a practical point of view it is apparent that the investigator in the instance of each disease can have only a finite number of cases. Although the results based upon a relatively small number of cases are often inconclusive, two purposes may be served in reporting them. The findings may indicate the need for collection of more data or, when they are added to series already collected, may result in convincing evidence of a previously suspected association. Conversely, a previously suspected association may be made less acceptable. A real danger exists, however, of drawing unwarranted conclusions from series of insufficient size, serving thereby to confuse and discredit these researches.

The findings concerning gastric cancer, peptic ulcer, and pernicious anemia support the attractive hypothesis of a relationship between the ABO blood groups and the pathological physiology of the stomach and duodenum in these patients. The evidence of a relationship to the secretion of free hydrochloric acid [10] fits nicely with this concept. It remains to be proved that ulcerogenic and carcinogenic or, conversely, protective attributes are exercised by the mucopolysaccharide blood group substances.

The evidence of associations for diseases not related to the gastrointestinal tract suggests that the association of blood group and disease may be related to broad anatomic, biochemical, and physiological considerations, thus relating disease and heredity. A possible role in natural selection is suggested for the ABO blood groups by these findings. Whether these and other speculations have basis in fact must await the collection of more data, with careful adherence to the criteria that have been established, and the results of basic investigations of the underlying mechanisms. Although the possibility that the findings merely indicate a chance association between the ABO blood groups and disease rather than a causal relationship becomes less likely with the report of each group of data confirming the association, the former possibility has not as yet been excluded. Likewise, an anthropological explanation based on the possibility that there are population strains with high or low incidences of certain diseases becomes progressively less tenable with the accumulation of similar data from different population groups throughout the world.

Summary

Conclusive evidence of an association between the ABO blood groups and disease has been found. Gastric carcinoma occurs more frequently in persons with blood type A than in those with the other blood types, peptic ulcer more frequently in those with blood type O, and pernicious anemia more frequently in those with blood type A. No evidence of such an association was found in patients with carcinoma of the colon and rectum, leukemia, ulcerative colitis, or those with congenital anomalies. In cancer of the lung and breast, more data will need to be collected before the equivocal findings may be properly interpreted; in view of the failure of other investigators to find evidence for an association, much more convincing data must be collected before the possibility of associations for these diseases may be claimed.

Addendum

Since this article was submitted for publication, in addition to the associations for gastric carcinoma and pernicious anemia we have found evidence of associations between rheumatic heart disease, hip fracture, and the ABO blood groups. Evidence has also been found of similar associations in a Negro population group.

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PEPTIC ULCERATION AND ABO BLOOD GROUPS

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• *The incidence of the four blood types O, A, B, and AB was studied in 1,301 patients with duodenal ulcer, 469 with gastric ulcer, and 69 patients with both gastric and duodenal ulcers. The three distributions so obtained were compared with the distribution found in a reference of 8,767 people without ulcers. Type O was more frequent among the ulcer patients than in the reference group, and calculations of probability showed that the association between type O and peptic ulcer was statistically significant. It was shown not to be secondary to any influences of sex, age, rhesus blood type, or occupation. Among a group of 529 patients who had histamine tests, however, the frequency of type O was significantly greater among those who reacted with an increase of free hydrochloric acid than among those in whom no increase of acid occurred.*

In 1921, 21 years after Landsteiner's [1] classic blood-group work, Buchanan and Higley [2] reported a study of the possible relationship of the ABO blood groups to various diseases, including peptic ulceration. These authors concluded that there was no relationship to any disease for which sufficient data were available to justify a conclusion. The data reported by Ugelli [3] in 1936 and Lessa and Alarcao [4] in 1949 show an increased (higher than expected) frequency of blood type O in patients with peptic ulcer. The failure to recognize the significance of these data may be attributed to the difficulty in obtaining suitable population control groups, a preoccupation with the study of multiple diseases, the small size of the series, and a failure to apply suitable methods of statistical analysis. In 1954, Aird and co-workers [5] demonstrated convincingly that a highly significant relationship exists between peptic ulceration and the ABO blood groups in Great Britain. Their data indicate that persons with blood type O are about 35% more likely to develop peptic ulceration than are those with the other types. Similar findings have since been reported by Clarke and associates [6] from Liverpool and Køster, Sindrup, and Seele [7] from Denmark.

The initial effect of these observations has been to give interested clinical and basic investigators alike a sense of fulfillment of the expectation, based on genetic considerations, that the relationships between diseases and blood groups that should exist, do in fact. Ford [8] hinted at this in suggesting the possible relationship of blood groups to natural selection. It is possible that a door has opened through which a way may be seen to further research leading to the solution of heretofore unfathomable problems related to the broad considerations of disease and heredity. As yet, satisfactory explanations for the observed phenomena have not been provided. The immediate need is for the collection of similar data from other population groups throughout the world. The present report concerns such investigations carried out in the United States; the authors of two previous reports from this country concluded that there was no association between the ABO blood groups and peptic ulceration.[9]

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Materials and Methods

The bulk of the clinical material for this study was provided by patients admitted to the University Hospitals from 1940 to 1956. Five other Iowa hospitals provided the remainder. Data obtained from the Iowa City and Des Moines blood banks have been used to determine the frequency of blood types in the population from which the patients came. Since the percentage of Negroes among the blood donors did not differ significantly from the 2.1% noted among the otherwise Caucasian patient groups, race did not contribute to the observed differences in blood-type frequency. In table 1, columns A and B, are recorded the number of individuals of each blood type and the percentage of the total group this number represents (subsequent-

ly referred to as blood-type percentage). Since there were no significant differences noted between the Iowa City and Des Moines donors in regard to the ABO group frequencies, they have been pooled and are henceforth referred to as controls (column C). A further indication of the reliability of these donor

TABLE 1.—*Blood-Type Distribution in Groups Studied*

Blood Type	A University Hospitals Donors		B Des Moines Donors		C Controls*		D University Hospitals Patients†	
	No.	%	No.	%	No.	%	No.	%
O	2,149	45.8	743	45.8	2,902	45.8	1,121	45.8
A	1,953	41.7	672	41.4	2,635	41.6	1,000	40.8
B	423	9.0	147	9.1	570	9.0	246	10.0
AB	165	3.5	61	3.7	226	3.6	84	3.4
Total	4,690	100.0	1,623	100.0	6,313	100.0	2,454	100.0

* Combined data (Cols. A and B).
† Patients with peptic ulcers or neoplasms excluded.

groups as representative population samples is provided by a comparison of the blood-type frequencies noted with those of a random sample of patients at University Hospitals, with only those with peptic ulcer and neoplastic disease excluded (table 1, column D). Statistical analysis of these data has been completed by methods to be described.

To ensure reliability of the data, it was essential to establish sound diagnostic criteria, which were then painstakingly applied in the selections of the cases. Either an anatomic or an ironclad clinical diagnosis of peptic ulcer was required. In the patients with

TABLE 2.—*Type of Ulcer, Blood Type, and Hospital of Patients Studied.*

Ulcer	Blood Type	Hospitals: Iowa City: University	Iowa City: Veterans*	Iowa City: Mercy	Des Moines: Methodist	Des Moines: Broadlawns	Total
Duodenal	O	382	155	66	58	43	698
	A	550	110	45	42	25	472
	B	53	26	10	9	4	102
	AB	16	7	1	3	2	29
	Total	701	298	122	106	74	1,301
Gastric	O	175	30	17	15	11	248
	A	117	20	19	14	13	183
	B	18	2	3	2	1	26
	AB	10		1	1		12
	Total	320	52	40	32	25	469
Duodenal and gastric	O	24	4	6	1	2	37
	A	15	3	5	1		24
	B	4		1	1		6
	AB	1			1		2
	Total	44	7	12	4	2	69
Totals	O	581	189	89	68	56	983
	A	682	133	69	57	38	679
	B	75	28	14	12	5	134
	AB	27	7	2	5	2	43
	Total	1,065	357	174	142	101	1,839

* Data from Iowa City and Des Moines veterans hospitals combined.

anatomic diagnoses, comprising more than 80% of the clinical material, the diagnosis was established at the time of operation by gross and/or microscopic findings. The surgeon's operative note and pathologist's reports were the source of this information. Differentiation of duodenal from gastric ulcer was similarly determined; a third group of patients having both duodenal and gastric ulcers was included. Patients having lesions located at the pylorus, in whom it was impossible to determine whether the ulcer was duodenal or gastric, were excluded. By ironclad clinical diagnosis is meant a convincing history and positive evidence of ulcer on radiological and/or gastroscopic examination.

To eliminate possible errors resulting from collection by multiple investigators, a team composed of three of us (E. B. W., D. C. C., and J. A. B.) selected and recorded all the data. On a separate card for each patient was recorded the desired information culled from the patient's case record. This included the following: identifying information, age, year seen, sex, race, occupation, primary and secondary diagnoses, method of diagnosis and treatment, gastric acidity, histamine-test response, Rh blood type, and, most im-

TABLE 3.—*O-A and O-A-B-AB Comparisons for All Patients with Ulcer*

Ulcer	Blood Type	Patients: No.	Patients: %	Difference in % from Controls	X^2	Level of Significance (Probability)
Duodenal	O	698	53.7	+7.9	20.340	$p<0.001$
	A	472	36.3	−5.3	29.573	$p<0.001$
	B	102	7.8	−1.2		
	AB	29	2.2	−1.4		
	Total	1,301	100.0	0.0		
Gastric	O	248	52.9	+7.1	4.206	$0.05<p<0.05$
	A	183	39.0	−2.6	12.995	$0.001<p<0.01$
	B	26	5.5	−3.5		
	AB	12	2.6	−1.6		
	Total	469	100.0	0.0		
Duodenal and gastric	O	37	53.6	+7.8	1.641	$p>0.10$
	A	24	34.8	−6.8	1.662	$p>0.10$
	B	6	8.7	−0.3		
	AB	2	2.9	−0.7		
	Total	69	100.0	0.0		
All ulcers	O	983	53.5	+7.7	23.256	$p<0.001$
	A	679	36.9	−4.7	37.049	$p<0.001$
	B	134	7.3	−1.7		
	AB	43	2.3	−1.3		
	Total	1,839	100.0	0.0		

portant, the ABO blood group. Innumerable correlation studies were made feasible by the transference of the collected data to IBM punch cards and the use of machine tabulation and sorting methods.

The only factors affecting case selection were our diagnostic criteria and the availability of blood-typing information. Through the record room files of the respective hospitals, the records of all patients with a diagnosis of peptic ulcer were scrutinized. Only one in six patients with a clinical diagnosis met our requirements and could be included in the study. In examination of the data, comparison has been made of the frequency of each blood type observed in the disease and control samples. The statistical significance of observed differences has been tested by the chi-square method, which naturally weights the disease to match the size of the control group. Aird and co-workers [5] have amply discussed the importance of this latter

calculation in making most efficient use of the data at hand. The validity of the analyses has been further tested by application of the method of differences in percentages based upon the normal curve theory.

Results

In table 2 are recorded the numbers of patients, tabulated by hospital and lesion, with each blood type. Comparison of the data collected from the individual hospitals, with the exception of the University Hospitals, would appear to be meaningless because of the small numbers of patients. No significant degree of heterogeneity was shown to exist between the hospital groups. Therefore, in the further examination of the data, those data from the six hospitals have been combined and are considered as one sample.

TABLE 4.—*Blood Types O and A with Reference to All Patients with Ulcers and to Controls*

	Blood Type			
	O	A	Totals	Type O, %
All ulcers	983	679	1,662	59.15
Controls	2,892	2,625	5,517	52.42
Totals	3,875	3,304	7,179	

The blood-type frequencies observed in patients with duodenal, gastric, and both ulcers were compared with those of the controls. For those who desire to do so, gene frequencies may be calculated by Fisher's method as described by Dodson and Ikin,[10] which is merely another way of presenting the data showing the same relationships. In table 3 are recorded the numbers of patients with each blood type by lesion, blood-type percentages, the increase or decrease of blood-type percentage of the disease as compared with the control group, chi-square values for the O-A and the O-A-B-AB comparisons, and the levels of significance indicated. A reciprocal difference is observed in the relative portions of the O and A types. When the data were analyzed by O-A, O-A-B, O-A-B-AB comparisons, etc., it became apparent that the simplest, most practical method of analysis was to study the significance of the reciprocal changes noted in the O and A blood-type frequencies. This is because the greatest discrepancies occur in blood type O and also because about 85% of the patients have either O or A blood type. Since this type of analysis has been used by previous workers, it also affords an opportunity to compare our results with those of similar studies being reported from different areas of the world. Since the other comparisons added little interest to the present discussion, only two results are recorded in the table, namely (1) the relative frequencies of types O and A and (2) the relative frequencies of types O, A, B, and AB.

For an example, suppose we examine the relationship of the blood types O and A with respect to ulcers of all types (table 4).

The calculation (1,662)(3,875)/7,179=897 shows that, if there were no relationship between blood group and ulcers, in a sample of this size one would expect to find ulcers in 897 patients of type O, purely as a matter of chance. In reality there were 983. The difference between the actual and the expected figures is therefore 86. The probability that so great a difference might occur simply as an accident of sampling is found by the following computation of chi square:

$$X^2 = \frac{[(983)(2,625) - (679)(2,892)]^2 (7,179)}{(1,662)(5,517)(3,875)(3,304)} = 23.26$$

A 2×2 contingency table has one degree of freedom. From tables of chi square one obtains, for 1 degree of freedom and a chi-square value of 23.26, a value of p less than 0.0005. This means that it is extremely unlikely that the above difference arose purely by chance; the difference is highly significant. We therefore assert that the incidence of ulcers of all kinds was significantly higher in patients with type O than type A blood, or that the incidence of type O among patients with ulcers of all kinds was higher than among the controls. This result is confirmed by the use of method of differences in percentages based upon the normal curve theory:

$$t = \frac{0.5915 - 0.5242}{\sqrt{\frac{(0.5915)(0.4085) - (0.5242)(0.4758)}{1,662} + \frac{}{5,517}}} = \frac{0.0673}{0.0138} = 4.88$$

which again is highly significant since the value of t is greater than 3.

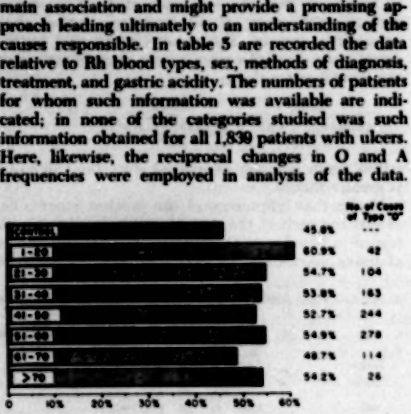
Notice that differences of the greatest magnitude, similar for each of the patient groups, occurred with regard to blood type O. Note the negative differences of lesser magnitude for the other three blood types in each group of patients. Disparity in the size of samples of patients is chiefly responsible for the differing levels of significance (probability) for the three groups, and it is possible that, if a comparable number of patients with gastric or both gastric and duodenal ulcers had been available, significant differences comparable to that for duodenal ulcer might have been observed. In the succeeding treatment of the data concerned with the specific characteristics of the groups of patients, the patients with duodenal, gastric, and both

TABLE 5.—*O and A Blood Types with Regard to Various Factors*

Row	Factors		Patients No.	Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
1	Rhesus +		1,228	O	626	52.3	+7.5		
				A	444	38.7	−5.4		
	Rhesus −		245	O	126	51.5	+5.7	0.882	p>0.10
				A	98	40.0	−1.6		
2	Men		1,194	O	627	53.4	+7.6		
				A	449	37.6	−4.0		
	Women		276	O	127	46.0	+10.7	0.849	p>0.10
				A	97	34.9	−6.7		
3	Anatomic diagnosis		1,540	O	834	54.1	+8.3		
				A	553	35.9	−5.7		
	Clinical diagnosis		299	O	151	50.5	+4.7	2.591	p>0.10
				A	124	41.5	−0.1		
4	Surgical treatment		1,372	O	740	53.9	+8.1		
				A	504	36.7	−4.9		
	No surgical treatment		429	O	224	52.2	+6.4	0.161	p>0.10
				A	169	37.3	−4.2		
5	Free hydrochloric acid	high	561	O	292	57.1	+11.3		
				A	209	38.0	−5.6		
		low	223	O	116	52.0	+6.2	1.254	p>0.10
				A	89	39.5	−2.7		
6	Hydrochloric acid high with operation		521	O	297	57.0	+11.2		
				A	167	33.9	−5.7		
	Hydrochloric acid low with operation		191	O	101	52.9	+7.1		
				A	70	39.8	−1.8		
	Hydrochloric acid high without operation		60	O	35	58.3	+12.5	1.686	p>0.10
				A	22	38.7	−4.9		
	Hydrochloric acid low without operation		32	O	14	43.8	−2.0		
				A	13	40.6	−1.0		
7	Free hydrochloric acid increased		414	O	220	55.6	+9.8		
				A	149	36.0	−5.6		
	After histamine not increased		115	O	49	47.6	+2.8	4.443	0.05<p<0.05
				A	51	44.3	+2.3		

ulcers have been combined and are considered as one sample. This was desirable not only because it simplifies the presentation but also because the possibility that a statistically significant relationship would be missed as a result of insufficient numbers of patients in a sample was thus reduced. When indicated, independent analyses for each group were done.

In view of findings that indicated an association between peptic ulcer and the ABO blood groups, it became important to explore the possibility that certain characteristics of these patients might have a relationship to the demonstrated association. Such a relationship would offer additional support for the main association and might provide a promising approach leading ultimately to an understanding of the causes responsible. In table 5 are recorded the data relative to Rh blood types, sex, methods of diagnosis, treatment, and gastric acidity. The numbers of patients for whom such information was available are indicated; in none of the categories studied was such information obtained for all 1,839 patients with ulcers. Here, likewise, the reciprocal changes in O and A frequencies were employed in analysis of the data.



Percentage of patients with peptic ulcer with blood type O, by decade of age. The frequency of type O among patients of all ages was 53.5%, while it was 45.8% for the controls.

Changes in B and AB frequencies were as expected; the analyses of the B and AB changes added nothing to our present considerations and are not recorded.

Of the 1,473 patients in whom the Rh blood type was determined, 1,228, or 83.4%, were Rh positive; when this was compared with the 84.3% noted in the controls, no significant difference was found. When the same analysis was performed for each blood type, i. e., comparison of positive and negative in patients and controls with blood type O, etc., no significant difference was found. These data were examined in another way in row 1, where the ABO blood-type frequencies noted within the positive and negative groups were compared; again, no significant difference was demonstrated. It may be concluded that Rh type appears to have no relationship to the ABO blood group–peptic ulcer association.

With those from the two Veterans Administration hospitals excluded, there remained 1,472 patients, of which number 1,194, or 81.1%, were men. Row 2 shows that there was no significant relationship between sex of the patient and the ABO blood group–peptic ulcer association. As has been stated, in addition to the bulk of patients with diagnoses established at the time of surgery, those with ironclad clinical diagnoses were included. Although comparison of these two groups, in row 3, indicates a higher frequency of blood type O in those patients with surgical diagnoses, no significant difference was demonstrated. Likewise, none was found when patients treated with and without surgery were compared (row 4).

Information concerning gastric analysis, specifically that concerned with free hydrochloric acid, was obtained for 804 patients. After scrutinizing the data regarding degrees of free acid, we decided that the most meaningful method of analysis was to compare those patients with decreased or negligible amounts of free acid and those with normal or increased amounts. Row 5 shows that the apparent differences in blood-type frequencies do not indicate a significant difference. When these two groups of patients are subdivided into those treated with and without surgery, in row 6, it is of interest to observe the O and A frequencies similar to those of the controls in the small group of patients with low acid and no surgery; no statistical significance was demonstrated in the analysis of the four subgroups; 3 degrees rather than 1 degree of freedom were present. When the 529 patients who had histamine tests performed are studied (row 7), there is seen to be a significant difference, indicating that those having an increase in free acid, as compared with those having no increase in free acid, have a stronger association between the ABO blood groups and peptic ulceration. When the blood-type percentages of the patients with ulcers were examined by decade of age, nothing was found to suggest a relationship of age to the ABO blood groups–peptic ulcer association. This is illustrated in the figure by the absence of significant differences in blood type O frequency when the various decades are compared; similarly, no significance was noted for blood types A, B, and AB. Occupation and social and economic status were studied and appeared equally devoid of significance.

Comment

Of the foremost importance in the interpretation of the findings of this study is the degree of homogeneity or heterogeneity of the controls and patients. In this respect, a relatively stable agricultural population would seem to have advantage in providing source material, as compared with the constantly shifting population found in metropolitan and urban areas, which must necessarily result in relatively more heterogenous groups of controls and patients. Our controls and patients were relatives or friends, with similar genetic, ethnic, and anthropological origins, coming from the same geographical region. A relatively insignificant number of first-generation and second-generation immigrants, from other countries or from elsewhere in the United States, are included. Evidence of the high degree of homogeneity is provided by similar blood-type frequencies observed in the two groups of blood donors and the similar findings noted in an unselected group of patients, with only those with peptic ulcer and neoplastic disease excluded. The use of patients from several hospitals with similar facilities and standards of clinical prac-

tice and drawing their patients from the same population group would seem to reduce the chance that the results would be distorted by screening factors related to any one hospital.

The most important single point that emerges from this study is the close agreement of the findings with those previously reported. The level of statistical significance of the association between peptic ulceration and the ABO blood groups is of the same high degree reported by Aird and associates [6] and Clarke and associates [8] in Great Britain and Køster, Sindrup, and Seele [7] in Denmark. Since the Iowa population is derived chiefly from northern European stock, rather minor anthropological differences probably exist between the samples studied. However, in table 6 it will be noted that real differences in blood-type frequencies in controls do exist; for example, of British and Danish controls, 47.1 to 49% and 40.6%, respectively, had blood type O. With each new population group studied, the attractive hypothesis that the findings have an anthropological basis related to population strains with high and low incidence of certain diseases becomes less tenable. However, it may be abandoned only if the results of similar studies conducted in anthropologically dissimilar populations confirm the reported findings. Such studies would also provide strong evidence that there is causal relationship between the ABO blood groups and peptic ulceration rather than just an association.

Our failure to find significant differences between patients with duodenal and gastric ulcers is in sharp disagreement with the findings of Clarke and coworkers [8] and to a lesser extent with those of others. Our findings of a relatively higher frequency of type O than was found by the other workers in gastric ulcer, coupled with a relatively decreased one in duodenal ulcer, are of interest. In table 6 are recorded the data reported by the various investigators (macroscopic diagnosis of duodenal and gastric ulcer) showing the increase or decrease in blood-type percentages of patient groups as compared with the control group. In view of the close agreement noted in duodenal ulcer, it is difficult to find a plausible explanation for the differences observed for gastric ulcer. The accumulation of additional data from these and other sources should ultimately provide the answer to this question.

Of the many avenues that suggest themselves for study, one of the most promising would seem to be the study of the possible relationship of the secretion of blood-type substances. Such data should permit testing of the hypothesis of the possible protective or ulcerogenic effects exercised by these substances upon the mucous membranes of the stomach and duodenum. The possibility exists that as yet undiscovered red blood cell or other associated and similar antigens linked to known type-specific substances may act locally or systemically, being responsible for the findings. Our results suggest that ulcer patients with higher levels of free hydrochloric acid have higher frequencies of blood type O than those with lower acid levels; this could be related to local tissue factors or to more fundamental individual differences. The findings of Struthers [11] and McConnell,[12] as well as our own findings,[13] suggest the existence of similar relationships between the ABO blood groups and disorders other than those of the gastrointestinal tract. This may be a clue suggesting that we are dealing with basic anatomic, biochemical, and physiological differences related to the genetic make up of the individual and, thus, linked to the ABO blood group.

The findings relative to the various clinical characteristics studied are difficult to interpret. Although statistical significance has been shown to exist only for the histamine studies, the total findings related to gastric acidity suggest a relationship here and indicate a need for the collection of more data. In view of a chi-square value approaching a level of significance when comparison of those patients with clinical and surgical diagnoses is made, it is of interest to speculate regarding the possible meaning of these findings. The most interesting and challenging suggestion is that this may be evidence that the ulcer diathesis is more severe in patients with type O than any other type, leading more often to surgical therapy. More probable is the possibility that not all clinical diagnoses were ironclad and thus an unknown number of patients without ulcer were included, lowering the frequency of blood type O in the group with clinical diagnoses. Collection of more data should provide more satisfying answers regarding the possible relationship of these clinical characteristics to the ABO blood groups–peptic ulcer association.

At this time, the explanation for and meaning of the observed association between peptic ulceration and the ABO blood groups remains in the realm of speculation. Although the current evidence does not permit any conclusions to be drawn regarding the possible relationship of these findings to the etiology and pathogenesis of peptic ulceration, a promising new territory has been opened up, exploration of which may ultimately provide some of the long-sought an-

TABLE 6.—*Data Regarding Macroscopically Diagnosed Duodenal and Gastric Ulcers Reported by Several Investigators*

Investigator	Blood Type	Duodenal Ulcer No.	Duodenal Ulcer %	Controls, %	Difference in % from Controls	Gastric Ulcer No.	Gastric Ulcer %	Controls, %	Difference in % from Controls
Aird and others[6]	O	1,048	56.6	47.1	+9.5	538	53.0	46.9	+6.1
	A	616	33.3	40.9	−7.6	376	37.0	41.1	−4.1
	B	141	7.6	9.0	−1.4	77	7.6	8.9	−1.3
	AB	46	2.5	3.0	−0.5	24	2.4	3.1	−0.7
Total		1,851	100.0			1,015	100.0		
Clarke and others[8]	O	505	58.7	48.9	+9.8	185	49.1	48.0	+0.1
	A	263	30.6	39.1	−8.5	153	40.1	39.1	+1.0
	B	62	7.2	9.5	−2.3	31	8.2	9.4	−1.2
	AB	30	3.5	2.5	+1.0	10	2.6	2.5	+0.1
Total		860	100.0			377	100.0		
Køster and others[7]	O	342	50.3	40.6	+9.7	136	40.3	40.6	+5.7
	A	301	39.4	44.0	−5.6	139	41.2	44.0	−2.8
	B	60	8.8	10.9	−2.1	28	8.3	10.9	−2.6
	AB	17	2.5	4.5	−2.0	14	4.2	4.5	−0.3
Total		680	100.0			337	100.0		
Present study	O	509	54.4	45.8	+8.6	231	53.5	45.8	+7.7
	A	370	35.3	41.6	−6.3	164	37.9	41.6	−3.7
	B	85	8.1	9.0	−0.9	25	5.8	9.0	−3.2
	AB	23	2.2	3.6	−1.4	12	2.8	3.6	−0.8
Total		1,047*	100.0			432*	100.0		

* The discrepancy with table 3 results from the exclusion of patients with ulcers in whom the diagnosis was established by nonsurgical methods.

swers to these and other equally pressing questions. As noted in our preliminary report,[14] the findings do suggest that the ABO blood groups may well participate in the process of natural selection.

Summary

In a comparison of the frequencies of the ABO blood types of 1,839 patients with duodenal and/or gastric ulceration with those observed in a representative sample of the population from which the patients came, a highly significant association was noted to exist between the ABO blood groups and peptic ulceration, characterized by an increase in O and reciprocal decreases in the three other blood-type frequencies; the findings are similar for duodenal and gastric ulceration. The level of free hydrochloric acid and whether the diagnosis was anatomic or clinical may possibly have a definite relationship to the association observed, while sex, age, rhesus blood type, and occupation appear to have none.

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EXPERIENCE WITH ARTERIAL HOMOGRAFT BANK

REPORT OF ONE HUNDRED CONSECUTIVE ARTERIAL HOMOGRAFTS

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• An arterial homograft bank was established to supply freeze-dried segments of human arteries for use in surgery. Analysis of the results from the first 100 preparations used shows that 36 were used in repairing aneurysms of the abdominal aorta and 24 in relieving arteriosclerotic obstruction in peripheral arteries, with results considered good in 24 and 20 cases respectively. Uniformly good results were obtained in 13 cases of obstruction of the terminal portion of the aorta and 11 cases of coarctation. Mortality was high in ruptured, but low in unruptured, aneurysms of the abdominal aorta. The preparation of materials for the arterial homograft bank can be undertaken by large community hospitals without additional highly trained personnel.

Many of the technical surgical procedures requiring the use of arterial homografts and the maintenance of arterial homograft banks can easily be provided by large community hospitals without additional highly trained personnel. To encourage others to establish similar banks, the following experiences are presented. An artery bank was first established at the Hospital of the University of Pennsylvania in 1953. A description of methods of preservation that have been used and an analysis of the results of the first 100 consecutive cases in which grafts from this bank were used is presented. This bank has supplied the needs of the Hospital of the University of Pennsylvania and on request has now supplied grafts to 24 other hospitals in the surrounding area. These institutions are in turn asked to help in procuring other grafts.

Methods of Preservation of Grafts

When the bank was established, freeze-drying was selected as the method of preservation and a freeze-drying unit was built.[1] It was of simple construction (fig. 1), and the total cost of the equipment was less than $500. It has required essentially no maintenance. Originally the grafts were all obtained under sterile precautions from fresh cadavers free of infection or malignant disease and were then placed in lactated Ringer's solution, to which antibiotics were added. The grafts were then refrigerated until the freeze-drying process was started. The freeze-drying was accomplished by quick freezing in a mixture of acetone and dry ice, and then the grafts were dried for 36 hours at low pressure (50 to 150 μ Hg). The grafts were then stored in test tubes sealed with rubber stoppers and capped with sealing wax after evacuation of the tube to a pressure of approximately 150 μ.

In the last year this method has been modified in several ways. The grafts are no longer taken under sterile conditions, and any human arteries not showing gross abnormality are considered suitable. Before freeze-drying, the grafts are sterilized with a 1% solution of beta-propiolactone, according to the method

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developed by Szilagyi and co-workers.[2] Grafts are now kept in sealed glass tubes ridged in order that they may be snapped open easily when needed (fig. 2). These grafts are then reconstituted in 0.9% saline solution, and their branches are tied off with suture ligatures after reconstitution. Prior to the use of sterilization of the grafts, it had become exceedingly

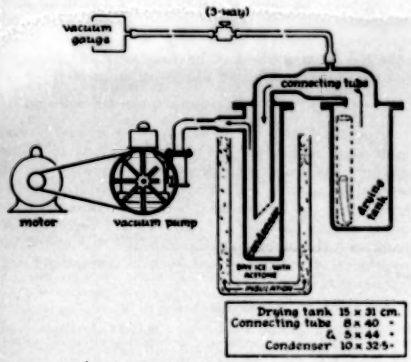

Fig. 1.—Diagram of freeze-drying apparatus.

difficult to obtain an adequate supply of grafts that fulfilled our criteria. Since the change in method of procurement and sterilization, some of these difficulties have been encountered with less frequency, and, as more interest has developed in the use of arterial homografts, it is becoming easier to obtain material.

The sealing of the grafts in glass ampuls has several advantages over the older method: the loss of vacuum that occurred in 10 to 20% of the test tubes when sealed with wax and rubber stoppers is prevented; the danger of contamination is reduced at the time the ampul is opened; and it is possible to sterilize the ampul itself by chemical means so that it can be handled freely by the surgeon. This procedure does, however, require the services of an

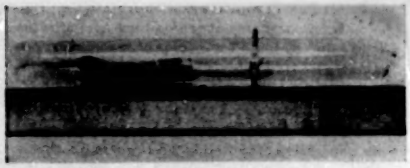

Fig. 2.—Freeze-dried artery stored in evacuated glass tube.

experienced glass blower, and, if such is not available, rubber stoppers and sealing wax can still be used to obtain a satisfactory seal.

Results with First 100 Grafts

In the table we have tabulated the results obtained from the use of the first 100 consecutive grafts from the bank. It has been possible to obtain follow-up data from every patient in whom they were used. The operative procedures were carried out by 17 different surgeons in 10 different hospitals, but 79 of the 100 grafts were used in the Hospital of the University of Pennsylvania. This table shows a representative cross section of the use of arterial homografts in vascular surgery today. In the analysis of these data we have listed results as good when there was definite improvement after the operation. For example, in patients with obstruction of the terminal portion of the aorta (Leriche's syndrome), if the circulation to both feet was improved after the operation the results have been called good even though pulses may not have been restored to the feet. The results have been listed as fair if the patient has been harmed in some manner even though the over-all result has been an improvement, i. e., after successful removal of an abdominal aneurysm, one patient had a small embolus that blocked one anterior tibial artery and he lost portions of three toes. When the operative procedure

Results Obtained from Use of 100 Arterial Homografts at Hospital of the University of Pennsylvania

Disease for Which Graft Used	Total	Good	Fair	Poor	Died
Aorta					
Abdominal aneurysms	36	24	1		11
Thoracic aneurysms	4	3			1
Coarctation	11	11			
Obstruction of the terminal portion of the aorta (Leriche's syndrome)	13	13			
Saddle embolus	1				1
Peripheral arteries					
Arteriosclerotic obstruction	24	20	1	3	
Aneurysm	4	3		1	
Tetralogy of Fallot (Blalock operation)	2	2			
Trauma	3	2		1	
Tumor	1	1			
Thrombosis, superior vena cava	1			1	
	100	79	2	6	13

resulted in further loss of circulation but not in death, the results have been listed as poor. The patients who died within 30 days after operation have been listed under the column "Died."

Examination of the results in abdominal aneurysms shows an operative death rate of 30%. Seven of the 11 deaths, however, occurred in nine patients with ruptured abdominal aneurysms—a group in whom the mortality is inevitably high. In the last 23 consecutive patients having unruptured abdominal aneurysms, there has only been one operative death—a mortality rate of less than 5%. The four patients who died after removal of unruptured aneurysms died of the following causes: (1) pulmonary embolus, (2) uremia, (3) myocardial failure after resuscitation of cardiac arrest while under anesthesia, and (4) rupture of the graft on the 28th postoperative day. This graft failure was the only one encountered in this series of 100 cases and occurred as a longitudinal split at the proximal suture line. There is some question about the reconstitution of this graft, in that it is believed to have been handled before it was completely reconstituted.

Among the patients having coarctation of sufficient length to preclude end-to-end anastomosis, the results of grafting have been excellent. Gross,[3] in a larger series, has also reported good results. We likewise have had satisfactory results in the use of these grafts in patients having the tetralogy of Fallot. Homografts

from the bifurcation of the aorta were inserted in 13 patients with obstruction of the terminal portion of the aorta, and all showed some improvement postoperatively.

In the table we have classified the common iliac arteries and any artery distal to them as peripheral arteries. By clinical evaluation, we have found only two late postoperative obstructions in the entire group, and many of the cases have been followed for from one to three years. This is in contrast to the report of Warren.[4] Of our two patients having late obstructions, one was operated on three months later because of thrombosis in another portion of his femoral artery and not in the graft. Another graft was successfully placed in his leg, and the pulse in his foot was again restored. The second patient has reverted clinically to her preoperative state, and additional procedures are contemplated.

Among the peripheral aneurysms that were replaced by grafts, three were in the popliteal artery and one in the femoral. The single poor result occurred in a popliteal artery graft. Of the grafts listed under "Trauma," two were for acute injuries in children, one of the popliteal artery and the other of the brachial artery. The latter graft was unsuccessful, since the arm was gangrenous at the time of operation. The remaining graft was used for an arteriovenous fistula of the subclavian vessels after a gunshot wound. The single patient listed under "Tumors" had a pelvic carcinoma that involved an iliac artery, which was removed and successfully replaced. Only readily available grafts make such unexpected procedures possible.

The replacement of diseased, obstructed, or injured major vessels has gained widespread acceptance, and grafting procedures will undoubtedly be done more frequently in the future. The relative merits of homografts versus prostheses are undetermined, and time alone can give us the answer to many of the controversies. It is our opinion that the majority of surgeons today prefer to use a homograft if a suitable one is readily available. The main objection to the use of homografts has been the difficulty of obtaining and preparing them. We believe that, if banks of the type described here were established in most large communities, homografts could be made available throughout the country and their use greatly increased.

Summary

Experience with the operation of an arterial homograft bank at the Hospital of the University of Pennsylvania has shown that procedures requiring use of arterial homografts and maintenance of arterial homograft banks can be provided by large community hospitals without additional highly trained personnel. A bank of arterial homografts increases the scope of treatment of arterial lesions such as arteriosclerosis, tumor, or trauma.

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HOW COMMUNICABLE ARE WARTS?

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• The distribution of warts was studied in an orphanage where 58 children lived during the winter months. Warts were found in 15. The warts in some instances had been present when the child arrived; in other instances they appeared some time after the child's arrival. There were cases of spontaneous disappearance and subsequent recurrence. The distribution of the lesions on different parts of the body did not afford clues as to the method of dissemination, and the time relations of their appearance were not clear. Four out of 18 adults resident in a seminary cottage reported warts; again it was difficult to interpret the data because information as to the time relations and the distribution among other residents was incomplete. Much work on the transmissibility of these lesions must be done before standard hygienic measures can be established. Better knowledge of this virus infection is very desirable because these lesions are so common. They affected at least 20% of the residents in the seminary cottage and more than 25% of the children in the orphanage.

As early as 1896 Jadassohn [1] pointed out that warts may be transmitted from one person to another. The occurrence and regression of these lesions has furnished a fascinating and abundant stock of folklore. Over many years various and sundry remedies have been recommended for the common wart. Nearly every small community has a "character" possessed of special abilities capable of "bewitching" off warts. For some reason the full moon has become important as a factor assisting in the removal of these lesions. Varied remedies have been suggested by lay persons from a list too long to transmit here. These suggestions often come from people who are otherwise apparently quite intelligent. A complete review of the folklore connected with warts would make a fascinating subject for a treatise. Those of us in dermatology hear these stories almost daily.

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Warts as a Virus Infection

Zwick [2] in 1932 made an interesting review of the subject. He states that the principle of physical disease being cured by suggestion is as dramatically presented with warts as with any disease we know. Bloch [2a] postulated an effect through the vegetative nervous system, causing an unfavorable medium for the virus and hence its death. It has been known, for some years now, that warts are a virus infection. This has more recently been pointed out by Strauss and coworkers [3] in their finding of virus-like particles and inclusion bodies in such skin lesions. They were found in some but not all warts. It is generally conceded by those interested in this field that several strains of virus are the etiological agents for various warts. That they are definitely communicable, however, has not been proved. Clinical reports of possible communicability of warts, therefore, would seem in order. There has been a marked paucity of such reports in the literature. The most pertinent one to the group under consideration here is a study by Grigg and Wilhelm [4] in 1953 on the epidemiology of plantar warts among school children. They examined all the children in the public schools of Dixon, Ill., over a period of one year. Of the students, 4.47% were found to have plantar warts. Incidentally, this study was done entirely with plantar warts and no particular study was made of the other types of warts present. As a control Grigg and Wilhelm checked the students in the neighboring village of Amboy, Ill. There they found 0.72% of the children had plantar warts. They felt the percentages were significant enough to be classed as of epidemic proportions. In a fairly carefully worked out comparison they found the following facts: 1. There was no relation to showers or foot baths. 2. Most of the lesions were multiple. 3. Of the warts, 86.7% were at pressure points. 4. Of the total student group, 10.28% had warts elsewhere on their body. 5. There was no difference in the incidence of plantar warts in other members of the family between children with plantar warts and those without plantar warts. Furthermore, Grigg and Wilhelm were unable to isolate a virus from the specimens they examined. These studies were done for them at the University of Michigan, Ann Arbor, Mich.

More recently an editorial [5] has pointed out that, in an examination of 13,000 school children in England, 9.71 children per 1,000 had warts. It is generally known that warts are much more common in girls than boys.[6] In some series,[7] this difference is four to five times as great. This is an interesting observation, for their presence previous to puberty would make it hard to relate to any endocrine activity. One author [8] theorizes that perhaps girls had more contact with bathroom floors than their brothers. Actually the reason for this sex difference is not known. Two-thirds of the cases occur in the age group 11-15.

Observation of Warts

After reviewing the subject and the major pertinent literature, it was deemed worthwhile to report the following group of cases seen in an orphanage over a period of about 18 months. It became apparent that there was an unusual number of patients with warts being brought to the office from this particular orphanage (it is unfortunate that all the inmates are girls). Two of them had been observed with warts several years previously. Twelve patients with warts of various types were observed over an eight-month period. In several other children there was a definite history of warts having been present previous to the ones seen in this present review. Furthermore, one or two of the patients had warts on entering the orphanage; however, by far the majority of them had been contracted after they came there, and no previous warts had been noted in these individuals (see table). Some 58 children are in this orphanage in the winter, while for the summer about 30 remain. Most of them have one parent or are from broken families to whom they can go during the summer when school is not in session. Therefore, the percentage of 25.8% is rough. On the other hand, there probably are several other children in the orphanage who were not seen and who have warts. I have heard this on rumor from some of the children. Furthermore, some of the children who have had warts that have spontaneously disappeared have never been brought in. While a few plantar warts were noted, the majority of the lesions were on other parts of the body, and, in one instance, the only lesion present was on the lip.

*Data on Fifteen Female Patients with Warts in an Orphanage Group**

Age, Yr.	No. of Warts	Location	Date Noted	Duration When Seen
11	8-10	Hands and left foot	2/13/55	2 mo.
15	2	Hand	7/6/55	3 wk. (had warts as child; cleared and recurred)
10	1	Lip	1/12/55	2 mo.
9	1	Palm of hand	7/6/55	4 mo.
13	4	Hand	3/20/55	2 yr.
10	8-10	Hands and leg	7/6/55	4 mo.
6	10-15	Hands and foot	2/13/55	3 mo.
10	1	Plantar on great toe	2/17/54	1 yr.
13	2	Index finger	5/9/55	3 mo.
13	1	Plantar on heel	12/15/55	4 mo.
15	1	Plantar on ball of foot	9/19/55	6 mo.
11	2	Hands	9/55	2 mo.
9	2	Hands	11/30/54	1 yr.
13	4	Hand	6/22/54	1½ yr. (had warts as child; cleared and recurred)
14	1	Thumb	5/10/55	4 mo. (present before entering orphanage)

*Children in orphanage: 58 in the winter and 30 in the summer. Of the winter group, 25.8% were involved.

I have recently observed, over a period of two weeks, three brothers and a priest from the same seminary with warts on their hands. The priest also had several lesions on his feet. The lesions were quite typical and, with one exception, had appeared since they entered the seminary. The first one to have the lesions was the priest. They lived in a cottage of a group of 18.

Comment

How often have we all seen several members of one family with warts? How significant are these findings? I do not think we can pass by the possible communicability of warts of all types. There are many factors known by all of us that point to their method of spread.

For instance, it is well known that combing the hair, shaving, and similar acts definitely transplant the virus, causing new lesions. However, the spread of lesions from one individual to another is a little more difficult to establish. Undoubtedly it does occur. Whether any precautions should be taken in institutions or schools to isolate individuals with warts is another matter. The consensus seems to be that this is not necessary. It may be, however, that, in institutions such as the seminary or orphanage, individuals with warts should observe some precautions. How strict these should be is difficult to say. Certainly a great deal more work must be done on the transmissibility of these lesions before one can establish such standards. It is not my purpose here to try to set up these requirements but merely to point out the possible communicability of this virus infection of the skin that, while similar to the average virus infection in many respects, also has some interesting differences.

Vaccines of wart tissue are ineffective in the therapy of warts. I tried this therapy in a series of cases, some years ago, using both human wart tissue extracts and wart vaccine prepared from the cow. The results were unsuccessful and never published. Veterinarians employ a wart vaccine in the treatment of lesions on cows that I understand is quite successful. Warts on cows apparently are an entirely different virus, with immune reactions equally as different. This merely helps point out the complexity of the problem as well as the lack of knowledge about the spread of one of the commonest of all diseases. There are probably a number of strains of the virus, some of which may be more communicable than others. This has been pointed out by Blank,[6a] and it may well be the explanation of the variability in apparent communicability of these lesions.

Summary and Conclusions

In two groups of institutional residents the incidence of warts was about the same. Of children in a certain orphanage, 25% developed warts over a one and one-half year period. About 20% of the inmates of a small seminary group did the same over a much shorter period. It is felt that some strains of wart virus are more communicable than others, although this has not been proved. Simple precautions may help to prevent the spread of warts.

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BLOOD ASCORBIC ACID LEVEL IN BIOFLAVONOID AND ASCORBIC ACID THERAPY OF COMMON COLD

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The incidence and course of common colds were followed in 89 medical students and nurses who volunteered in a study of the efficacy of naringin, a bioflavonoid extracted from grapefruit peel and used in remedies for colds. One group of 22 subjects received 333 mg. of naringin and 65 mg. of ascorbic acid three times daily for three months; a second group received naringin only, another ascorbic acid only, and the fourth a placebo. These substances were administered in capsules as nearly alike as possible. Symptoms of colds were systematically recorded, and the levels of ascorbic acid in the blood were determined periodically. The average level of ascorbic acid in 22 men who were to receive ascorbic acid by mouth was initially 0.96 mg. per 100 cc. of blood; after 12 weeks of taking only ascorbic acid the average for this group was 1.41 mg. per 100 cc. of blood. In all groups and at all stages, the blood ascorbic acid levels for males were significantly lower than those for females. There was no evidence that the naringin affected the ascorbic acid level of the blood, prevented colds, or cured them.

During the past year treatment with the bioflavonoids has been widely publicized as a means of preventing or modifying the common cold. One of the reasons given for the effect has been that they potentiated ascorbic acid (vitamin C) in alleviating cold symptoms. Since there was no convincing proof available, either in support or in denial, we undertook a pilot study to explore the validity of these statements. Within the limits of this study, the bioflavonoid tested showed effect neither on the incidence or cure of colds nor on the ascorbic acid content of the blood. In the course of the study, interesting data were developed regarding the relationship of blood ascorbic acid levels to the incidence and cure of colds. These are reported in detail.

Method

The study was made on 89 volunteer medical students and student nurses for the three-month period from February to May, 1956. Four groups were established and given capsules (three times daily,

From the Dartmouth Medical School and the Hitchcock Foundation.

orally) made up as follows: group 1, bland placebo; group 2, naringin (bioflavonoid), 333 mg., and ascorbic acid, 65 mg.; group 3, ascorbic acid, 65 mg.; and group 4, naringin (bioflavonoid), 333 mg. (Naringin is an extract of grapefruit peel.) Every effort was made to disguise the contents of the capsules. All looked

TABLE 1.—*Blood Ascorbic Acid Level Determinations in Group 1: Patients Given Placebo*

Patient No.	Sex	Level, Mg./100 Cc. Initial Wk.	6th Wk.	12th Wk.	During Cold	Wk. of Cold	Results of Treatment
1	M	1.07	0.60	1.20	0.80	5th	No change
5	M	1.04	1.32	1.60	1.36	5th	Improved
9	M	1.12	1.08	1.52			
13	M	0.72	1.08	1.80	1.24	7th	No change
					1.84	4th	Cured
17	M	1.12	1.12	1.10	1.32	4th	Improved
21	M	0.80	0.76	1.20			
25	M	1.00	1.28	0.88			
29	M	0.40	0.44	0.40			
33	M	1.12	1.16	0.44			
37	F	1.00	1.40	1.28			
41	M	1.36	1.32	1.44			
45	M	1.08	1.12	0.96			
49	M	1.08	1.28	1.10			
53	F	1.60	1.80	...			
57	F	1.20	1.20	...			
61	M	0.76	0.88	1.12			
65	F	1.00	1.16	1.08			
69	F	1.12	1.32	...			
73	F	1.44	1.40	1.40			
77	M	0.44	0.28	0.50	0.40	5th	Worse
81	F	0.52	0.70	1.34	0.80	6th	No change
85	F	1.48	1.64	1.12			
89	M	1.36	...	...			

and tasted alike. Even the doctors conducting the study did not know the key to the code numbers used. Groups were assigned in rotation. Thus the first volunteer in line received bland placebo, the second naringin (bioflavonoid) and ascorbic acid, and the fifth bland placebo, as the rotation started over again.

TABLE 2.—*Blood Ascorbic Acid Level Determinations in Group 2: Patients Given Bioflavonoid and Ascorbic Acid*

Patient No.	Sex	Level, Mg./100 Cc. Initial Wk.	6th Wk.	12th Wk.	During Cold	Wk. of Cold	Results of Treatment
2	M	1.12	1.48	2.00			
6	M	1.08	1.12	1.48	1.08	2nd	Cured
10	M	0.80	1.16	1.28	0.96	2nd	Cured
					1.16	6th	Worse
14	M	0.96	1.36	1.30			
18	M	1.12	1.60	1.38	1.12	1st	Improved
					1.20	4th	Improved
22	M	0.56	1.52	1.10			
26	M	0.72	1.28	1.20			
30	M	0.72	1.52	...			
34	M	0.96	1.60	1.30			
38	F	1.48	2.00	1.72			
42	M	1.12	1.48	1.30	1.60	4th	Cured
46	M	0.92	1.68	1.04			
50	M	1.08	1.44	1.50			
54	F	1.40	1.84	...			
58	F	1.36	1.84	1.38			
62	F	1.84	1.64	...			
66	F	1.40	1.56	1.72			
70	F	1.88	1.76	1.56			
74	F	1.48	1.44	1.84			
78	M	1.32	1.40	1.84			
82	M	0.96	1.48	...			
86	F	1.28	1.92	1.68			

Each subject received a regional physical examination and had blood taken for a determination of ascorbic acid level the day he started the study. All the volunteers were started on the regimen within a single week. Thereafter they continued taking their particular capsule for the three months of the study. At the 6-week and 12-week points in the study, determinations of blood ascorbic acid level were made on all 89 participants. The subject was instructed to report cold symptoms (such as coryza, headache, malaise, fever, or sore throat) the day of onset. At this time the physical examination and determination of blood ascorbic acid level were repeated. He was asked to take no specific cold remedies, not even aspirin or nasal sprays, during the course of the infection. He continued taking the same dosage of the capsule assigned to his group. No antibiotics were used. During the infection the same physician made a record (daily when possible) of the cold's progress or regression. On the fifth day the cold was evaluated as cured, improved, unchanged, or worse.

Two variables were accepted as calculated risks to the accuracy of the study: diet and individual reliability. Although the majority of the subjects ate in the same hospital cafeteria, precise control of their diet was felt to be beyond the scope of this essentially pilot study. We recognized, of course, the varying degrees of reliability with which 89 persons would take 3 capsules a day for three months; we believe, however, that close supervision and the medical orientation of the participants kept this factor of error at a minimum.

TABLE 3.—*Blood Ascorbic Acid Level Determinations in Group 3: Patients Given Ascorbic Acid*

Patient No.	Sex	Level, Mg./100 Cc. Initial Wk.	6th Wk.	12th Wk.	During Cold	Wk. of Cold	Results of Treatment
3	M	1.08	1.32	1.50	1.40	3rd	Improved
7	M	1.28	1.52	2.00	1.92	3rd	Cured
11	M	1.12	1.56	2.00	1.32	3rd	Cured
15	M	0.56	1.68	1.24	1.60	3rd	Improved
19	M	1.12	1.08	0.80	1.08	3rd	Cured
23	M	1.08	1.32	1.10			
27	M	0.72	1.28	1.40			
31	M	1.08	1.16	1.70			
35	M	0.72	0.96	...			
39	F	0.96	...	...			
43	M	1.12	1.48	1.30			
47	M	0.76	1.44	1.50			
51	F	1.36	1.28	...			
55	F	2.04	2.08	1.32			
59	F	1.32	1.28	1.30	1.68	1st	Cured
63	F	1.40	1.52	1.84	1.52	4th	Cured
67	F	1.28	1.72	...			
71	F	1.28	1.40	1.52			
75	F	1.12	1.56	2.72			
79	M	0.88	1.36	1.68	1.52	4th	Improved
83	M	0.96	...	...			
87	M	0.52	...	...			

Tables 1, 2, 3, and 4 give the detailed blood ascorbic acid levels accumulated during this study. They are included in their complete form, partly because they are the basis for the conclusions of this pilot study and partly because comparable records of blood ascorbic acid levels in normal young adults are relatively rare. (Ascorbic acid blood levels were determined according to the technique of Roe and Kuether[1] under the supervision of John P. Davison, Ph.D., assistant professor of the physiological sciences in the Dartmouth Medical School.)

Results

Table 5 summarizes the effectiveness of bioflavonoid with and without ascorbic acid. When used alone, it produced the same results as a placebo. When used with ascorbic acid, the results were comparable to

those with ascorbic acid alone. Table 6 indicates that the prolonged administration of bioflavonoid had no effect on the blood ascorbic acid level. Females consistently showed a higher blood ascorbic acid level than males (table 6—statistically significant at the 0.01 level). Most of those receiving ascorbic acid showed an increased blood ascorbic acid level. Those receiving ascorbic acid developed just as many colds as those not receiving it (table 5). In this small series, those receiving ascorbic acid showed more rapid improvement in their colds than those not receiving it (tables 1 to 5 inclusive—statistically significant at the 0.05 level).

Comment

Ascorbic acid deficiencies have been noted not only in classic scurvy but in other infectious and metabolic disorders, such as rheumatoid arthritis, rheumatic fever, tuberculosis, and certain virus infections. The importance of ascorbic acid in maintaining capillary integrity has long been recognized. We will discuss neither the related background nor the literature.

Table 4.—*Blood Ascorbic Acid Level Determinations in Group 4: Patients Given Bioflavonoid*

Patient No.	Sex	Level, Mg./100 Cc. Initial Wk.	6th Wk.	12th Wk.	During Cold	Wk. of Cold	Results of Treatment
4	M	1.20	1.28	1.20	1.28	5th	Cured
8	M	1.08	0.88	1.20			
12	M	0.72	1.20	1.20			
16	M	0.96	0.72	1.00	1.00	5th	Improved
					0.96	1st	Worse
20	M	1.08	1.08	1.00			
24	M	1.00	1.20	0.96			
28	M	1.12	1.08	0.80			
32	M	1.28	1.40	1.60			
36	M	0.88	1.08	1.20	1.00	3rd	Worse
40	M	1.40	0.88	1.30			
44	M	1.08	0.96	1.52	1.08	1st	Improved
48	M	1.28	0.76	1.20			
52	F	1.08	1.20	1.28	1.12	7th	Improved
56	F	1.75	1.64	...			
60	F	1.56	1.48	1.32	1.08	3rd	Improved
					1.20	5th	Worse
64	F	1.36	1.40	1.44			
68	F	1.80	1.84	1.60			
72	F	1.48	...	...			
76	F	1.72	1.84	...			
80	M	0.64	0.80	0.80			
84	F	1.24	...	...			
88	F	1.36	1.48	1.30			

Recently certain naturally occurring substances have been found to have a related function in maintaining the integrity of the intercellular cement substance. The materials as a group have been classified as flavone glycosides and include such substances as hesperidin, rutin, and naringin. We are particularly concerned with those substances derived from citrus fruit peels, grouped together under the title of bioflavonoids. The significant literature on this subject was summarized at a meeting of the New York Academy of Sciences in 1955, which is reported in the annals of that organization.[2] Various articles in this monograph suggest a relationship between ascorbic acid and the bioflavonoids, with particular reference to their effects on capillary fragility. The monograph also reports the clinical use of the bioflavonoids and ascorbic acid in the treatment of disorders related to decreased capillary permeability. These include poliomyelitis, rheumatic fever, and bleeding related to pregnancy. The hypothesis that the bioflavonoids may prevent or modify colds is apparently based on this same property.

With this possibility in view, a number of drug compounds appeared on the market during the winter of 1955-1956 featuring a bioflavonoid content. Most of these compounds also contained such old cold treatment stand-bys as aspirin, caffeine, and ascorbic acid. The limited statements regarding this treatment of colds reported the use of the whole compound, without reference to specific studies based on the effect of the bioflavonoid alone.

We are reporting a pilot study on the effectiveness of one bioflavonoid per se. It is, of course, not definitive. But, in the absence of any comparable evaluation of a material whose commercial distribution is already widespread, we feel that even this limited study may be helpful to the medical profession. The approximately 300 determinations of blood ascorbic acid level were a by-product of the bioflavonoid study. The series is far too small to warrant conclusive interpretations, but the data raise several points of interest that may serve as points of departure in more definitive studies.

Table 5.—*Incidence and Cure of Colds with Bioflavonoid and Ascorbic Acid*

Group	No. in Group	No. Colds in Group	Colds Cured or Improved in 3 Days
Placebo	23	7	3
Bioflavonoid plus ascorbic acid	22	6	5
Ascorbic acid	22	8	3
Bioflavonoid	22	8	4

Table 6.—*Average Blood Ascorbic Acid Level in Males and Females*

	Level, Mg./100 Cc. Placebo		Bioflavonoid Only		Ascorbic Acid Only		Bioflavonoid and Ascorbic Acid	
	M	F	M	F	M	F	M	F
Initial	0.95	1.32	1.06	1.48	0.98	1.32	0.98	1.56
6th wk.	0.89	1.33	1.04	1.55	1.25	1.55	1.20	1.76
12th wk.	1.12	1.58	1.12	1.43	1.41	1.72	1.20	1.63

Summary

We are reporting a controlled pilot study of the clinical effect of bioflavonoids and ascorbic acid (vitamin C) on the incidence and cure of the common cold, correlated with serial determinations of blood ascorbic acid level on the 89 medical students and student nurses comprising the test group. The administration of a bioflavonoid had effect neither on the incidence or cure of colds nor on the ascorbic acid level of the blood.

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Statistical analyses were done by J. Laurie Snell, assistant professor of mathematics, Dartmouth College.

All drug preparations were provided by the Nepera Chemical Co., Inc.

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USEFULNESS OF BIOFLAVONOIDS AND ASCORBIC ACID IN TREATMENT OF COMMON COLD

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• *The evaluation of any drug used to treat the common cold must necessarily be based on clinical observations. Bioflavonoids and ascorbic acid, singly and in combination, were evaluated in a study on almost 2,000 persons as to their efficacy, not by symptom alleviation but as to whether it would shorten the course of illness. The overwhelming impression gained from the study presented is the singular lack of effect in altering the course of the common cold by either the bioflavonoid or the ascorbic acid.*

The objective evaluation of a new form of treatment for the common cold has always proved difficult. Since the viruses causing it have thus far completely resisted all attempts at direct annihilation through the use of antibiotics, no bacteriological studies on the disappearance of the causative organism have proved feasible, nor have any other laboratory tests been found of great use in estimating the individual's rate of recovery. Therefore, the evaluation necessarily has been based essentially on clinical observations.

Basically, treatment of the common cold has been limited to the relief of symptoms, the prevention of complications, and the general and specific supportive therapies that enable the body's own defense mechanisms to overcome the disease. Because the illness is essentially self-limited, with serious complications developing in only a small proportion of cases, any therapy that alleviates the patient's symptoms is called a cure until the test of time reduces it to the level of the other drugs that make the patient more comfortable but do not appreciably affect the underlying cause of the disease. To postulate that a given drug has a specific effect upon the disease, therefore, it must be shown that it does more than relieve symptoms. It should shorten the course of the illness. Furthermore, since there are innumerable drugs that make the patient more comfortable and alleviate symptoms, thereby creating subjective evidence that they are affecting the course of the cold, a cold cure should have an effect over and above the best of these relief medications. Lastly, in view of the fact that the evaluation of effect is almost entirely clinical, and therefore subjective from the point of view of either the patient or the observer, the beneficial result of the drug should be demonstrable in a controlled experiment in which personal bias has been entirely eliminated.

In the past decade, much attention has been given to the treatment of colds by the use of drugs that would enhance the body tissue's resistance to invasion. This has been at least in part behind the rationale for the use of such agents as antihistamines.[1] Even more recently, the administration of ascorbic acid (vitamin C) has been advocated,[2] both to raise the general resistance and on the theory that viral invasion is a function of capillary wall permeability that could be reduced by raising the ascorbic acid levels in the blood. On the basis of this theory, ascorbic acid has been added to a number of preparations used for the treatment of acute upper respiratory infections. The most recent approach to the problem has been an extension of this theory. It has been noted that the citrus bioflavonoids enhance the effect of ascorbic acid in maintaining or restoring to normal the integrity of the capillary wall.[3] In particular, they have been reported as directly combating virus infections by preventing the micro-organisms from penetrating the capillary endothelium.[4] It has been logically argued, therefore, that the bioflavonoids can exert a beneficial effect on the body's ability to resist the invasion of respiratory viruses, and several observers have reported cases that appear to substantiate this claim.[4] Because of the widespread interest in this attack on the problem of the common cold, it was felt that a definitive test of these agents would be of considerable value.

Since it is admitted that neither ascorbic acid nor the bioflavonoids have any in vitro effect on respiratory viruses,[5] such a study would have to be entirely clinical. It would be necessary to prove either that an appreciable number of colds were aborted in their early stages or that some or all of the symptoms were cleared up significantly earlier. The effect looked for would be more than a temporary alleviation of symptoms and should therefore be demonstrable even in the presence of other medicaments given merely to that end. To avoid any possibility of observer bias, the trials should be made on a completely blind basis.

Methodology

Since the bioflavonoids were postulated as acting in conjunction with ascorbic acid, it was felt necessary to study the effect of the two substances both singly and in combination. An experimental design was used that would permit the evaluation of each compound independently and also would demonstrate any synergistic effect obtained. The trials were therefore conducted with the following four preparations: (1) 250 mg. of bioflavonoid (lemon bioflavonoid complex 497, Sunkist Growers) plus 50 mg. of ascorbic acid; (2) 250 mg. of bioflavonoid; (3) 50 mg. of ascorbic acid; and (4) placebo.

The subjects were divided into four groups, each of which was given one of these preparations four times a day. In order to demonstrate that any effect ob-

Medical Director, Sylvania Electric Products, Inc. (Dr. Tebrock) and Medical Director, Pratt-Whitney and Company, Inc., West Hartford, Conn. (Dr. Johnston).

served was more than that obtainable through standard palliative practice, every patient received a preparation containing 325 mg. of salicylamide, 195 mg. of acetophenetidin, 65 mg. of caffeine, and 50 mg. of thonzylamine hydrochloride. This was done so that a patient not receiving ascorbic acid or bioflavonoid or a combination was actually receiving medication, which, in addition, acted as a control.

ascorbic acid will be demonstrated using all the patients, since the two halves represent the same distribution except for the presence or absence of this factor. The patients indicated in the lower box of each half also receive bioflavonoid, but, since they are about the same proportion of the total, the effect of the latter will cancel out unless a marked synergism is present. The difference produced by bioflavo-

TABLE 1.—*Comparison of Eight Test Groups for Randomness of Distribution*

	Group 1 Without Flavonoid or Ascorbic Acid		Group 2 With Flavonoid and Ascorbic Acid		Group 3 Without Flavonoid and With Ascorbic Acid		Group 4 With Flavonoid and Without Ascorbic Acid		Group 5 Without Flavonoid or Ascorbic Acid		Group 6 With Flavonoid and Ascorbic Acid		Group 7 With Flavonoid and Without Ascorbic Acid		Group 8 Without Flavonoid and With Ascorbic Acid	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Sex																
Male	134	58.2	138	60.3	144	55.2	134	54.9	129	54.6	136	55.7	122	49.8	126	52.5
Female	116	46.8	91	39.7	117	44.8	110	45.1	110	46.0	108	44.3	123	50.2	114	47.5
Total	232		229		261		244		239		244		245		240	
Ages																
Up to 20	13		11		10		18		11		7		13		18	
21-25	38		47		37		45		49		49		41		42	
26-30	47		49		67		57		60		70		62		50	
31-35	64		48		45		66		44		41		44		57	
36-40	32		27		44		34		24		24		32		25	
41-45	26		17		22		23		22		23		21		20	
46-50	13		8		8		10		12		9		10		10	
51-55	10		5		9		9		7		14		4		8	
56 +	4		9		8		2		5		4		5		7	
Total	247		221		250		242		234		241		242		237	
Mean age	34.0		33.0		34.2		32.5		32.9		33.2		33.2		33.0	
Mean no. of colds per yr.	2.65		2.72		2.72		2.79		2.53		2.51		2.99		2.54	

Use of these four preparations enables one, by means of a square experimental design, to simultaneously compare the effect of two drugs, both separately and together, and yet to use all the patients in each of the comparisons. In figure 1, each of the boxes represents an approximately equal number of patients receiving the drugs indicated. The effect of

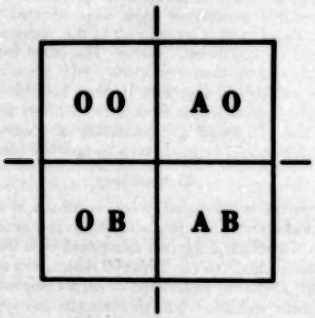

Fig. 1.—Diagram of square experimental design. O = placebo; A = ascorbic acid; and B = bioflavonoid.

ascorbic acid (A in fig. 1) could be evaluated by comparing the upper two boxes and that of bioflavonoid (B in fig. 1) could be evaluated by comparing the two left-hand ones, but this would utilize only half the patients for each evaluation. If, however, the patients in the left-hand side of the square are compared with those in the right-hand half, the effect of noid, irrespective of ascorbic acid, can be shown similarly by comparing the upper and lower halves. The amount of synergism or antagonism can be evaluated by determining whether the difference between OO (placebo) and AB is significantly greater or less than the sum of the difference between OO and AO plus OO and OB.

The trials were conducted on subjects reporting to several outpatient industrial clinics under the supervision of the physicians conducting the study. A num-

TABLE 2.—*Additional Diagnoses and Other Medications in Drug Groups*

Additional Diagnoses	Flavonoid				Ascorbic Acid			
	With		Without		With		Without	
	No.	%	No.	%	No.	%	No.	%
Pharyngotonsillitis	61	6.4	66	6.8	64	6.7	63	6.6
Tracheobronchitis	42	4.4	37	3.8	42	4.4	37	3.9
Antibiotic given	69	7.3	63	6.5	71	7.4	61	6.4
Nasal decongestant	135	14.2	123	12.7	133	13.9	125	14.1
Cough medicine	89	9.4	116	12.0	92	9.6	113	11.8
Pills not all taken	221	23.3	200	20.6	222	23.7	199	20.7
Total in group	947		969		956		969	

ber of college, seminary, and private patients of one of the authors were also included. Medicaments supplied to these physicians were identified only by number, so that neither they nor the patients were aware of what was being given. Furthermore, in order to reduce the possibility of the clinical judgments being influenced by continued association of better results with one of the preparations, each of them was supplied under two numbers, making eight test groups in all to which the patients were assigned in rotation.

Because it was not feasible to reexamine the subjects daily, a single checkup after three days was decided on. It was felt that, if colds were aborted to any appreciable degree by one or both of the drugs, the number of cures after three days should be appreciably higher than in the controls. At the same time, while some alleviation of symptoms was expected in all groups, the proportion should be materially increased in any group receiving an effective therapeutic agent in addition to the palliative medicament. The three-day limit was selected because, with a longer interval, too many cases might resolve spontaneously, while a shorter time would not afford a chance for disappearance of symptoms even under effective therapy. Since the dispensaries were in operation from Monday through Friday, only those cases first seen on Monday, Tuesday, and Friday were included in the study, in order to permit a return at the proper time.

Patients coming to the dispensaries or private offices on those days were first examined. If a diagnosis of an acute upper respiratory infection was made, patients were admitted to the study and assigned to one of the eight test groups in sequence. Their symptoms, physical findings, and other pertinent data were then recorded on a special printed form, which was precoded for machine punching and tabulation. The patient was given sufficient medicament to provide four doses a day for three days and instructed to report back at the end of that time. To simplify compounding and dispensing the medicaments, the ingredients that varied from group to group were put into one capsule, while those given to all groups were put in another. Cough medicine and nasal decongestants were also dispensed if indicated and were recorded on the form. In the case of the industrial patient, when secondary bacterial infection appeared to be developing, he was recommended to his personal physician.

Symptoms to be recorded were limited to eight considered most characteristic of the common cold: running nose, sneezing, hoarseness, cough, malaise, headache, postnasal drip, and sore throat. Only their presence or absence at the initial visit was noted, to avoid the difficulty of grading their severity. The time since the onset of the first symptoms was also recorded, as was the patient's temperature at the initial visit. The notation of physical findings was also limited to those associated with acute upper respiratory infections. Nasal secretions were reported as none, slight or marked, or mucoid or purulent and nasal obstruction as none, partial or complete, or unilateral or bilateral. Pharyngitis was graded as none, mild, moderate, or severe. The diagnoses of pharyngotonsillitis or tracheobronchitis were recorded if present.

TABLE 3.—*Subjective and Objective Change by Drug Groups*

	Bioflavonoid				Ascorbic Acid			
	With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%
Subjective								
Worse	110	11.7	122	12.5	111	11.6	121	12.6
No change	218	23.1	217	22.3	225	23.5	210	21.9
Improved	406	43.1	400	41.1	400	42.7	397	41.5
Cured	208	22.1	234	24.0	213	22.2	229	23.9
Total	942		973		958		957	
Objective								
Worse	79	8.4	93	9.6	85	8.9	87	9.1
No change	200	21.3	189	19.5	201	21.2	188	19.6
Improved	441	47.0	449	46.2	443	46.6	447	46.6
Cured	218	23.2	240	24.7	221	23.3	237	24.7
Total	938		971		950		959	

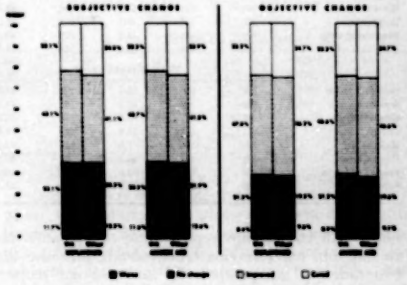

Fig. 2.—Subjective and objective change by drug groups.

At the examination on the third day, the presence or absence of the same symptoms was again recorded, and the physical findings were graded as before. The over-all change in the patient was evaluated, both subjectively and objectively, as worse, no change, improved, or cured. A note was made on whether the patient had taken all his pills and whether he had remained at work and on the number of days lost, if any. All these entries could be recorded on the study form simply by circling the appropriate finding under each heading.

Analysis of Results

Almost 2,000 individuals with acute upper respiratory infections between January and May, 1956, were used in the study. A small number were dropped for failure to report back on the third day, and a few study forms were not completely filled out, but the over 1,900 observations reported under all headings were a more than adequate sample to demonstrate any significant differences that might be produced by the drugs. The coded findings on each case were punched on IBM cards, which were then sorted by test group. These were tabulated for each observation and the distributions percentaged or converted to means. (Where appreciable differences in percentages or means were found, tests for statistical significance were made, using a chi-square test for percentage variations and a t-test for evaluating differences in means. Because of the many observations compared, differences were not considered significant unless the chance probability was 1% or less.)

Table 1 shows the distribution of the eight treatment groups by age and sex. The small differences noted were all accounted for by random sampling variation, and there were no statistically significant differences. The comparability of mean number of colds per year shown in this table indicates that the groups were also random with regard to patients' susceptibility to colds. These eight groups were com-

TABLE 4.—*Decrease in Symptoms by Drug Groups*

Symptoms	Total Patients	Present Initially No.	Present Initially %	After 3 Days	Decrease, %	Total Patients	Present Initially No.	Present Initially %	After 3 Days	Decrease, %	Difference in % Due to Drug
	With Flavonoid					Without Flavonoid					
Running nose	917	621	67.7	330	46.9	909	659	68.0	334	49.3	−2.4
Sneezing	917	534	58.2	165	69.1	909	579	59.8	156	73.1	−4.0
Hoarseness	945	352	37.2	163	53.7	982	396	39.3	181	53.1	0
Cough	945	408	43.0	320	21.2	982	463	47.1	348	24.8	−3.6
Malaise	929	444	47.8	160	64.0	962	493	51.2	166	66.3	−2.3
Headache	929	447	48.1	172	61.5	962	491	51.0	173	64.8	−3.3
Postnasal drip	949	325	34.2	193	40.6	979	316	32.3	186	41.1	−0.5
Sore throat	949	455	47.9	188	58.7	979	447	45.7	186	58.4	+0.3
	With Ascorbic Acid					Without Ascorbic Acid					
Running nose	926	650	69.4	339	47.0	930	640	67.4	325	49.2	−2.2
Sneezing	926	570	60.9	161	71.8	930	543	57.2	160	70.5	+1.3
Hoarseness	961	371	39.6	175	52.8	966	367	38.0	169	54.0	−1.2
Cough	961	432	45.9	329	23.9	966	437	45.2	339	22.4	+1.5
Malaise	944	444	47.0	145	67.3	947	466	49.1	161	65.3	+4.0
Headache	944	464	49.2	182	60.8	947	474	50.1	163	65.6	−4.8
Postnasal drip	968	335	35.0	201	40.0	970	306	31.5	178	41.8	−1.8
Sore throat	968	449	45.9	185	58.0	970	462	47.6	189	59.1	−1.1

bined into two groups representing the patients receiving and not receiving bioflavonoids, and also the two different groups that did and did not receive ascorbic acid. The following tabulations are presented for all these combinations. Table 2 gives further evidence of the statistical comparability of the groups. The percentage of patients with pharyngotonsillitis and tracheobronchitis was not significantly different from group to group. Roughly the same proportion of patients required additional medicaments in each group, including antibiotics, nasal decongestants, and cough medicine, in addition to the medicaments under test, and none of these additional medicaments was given in a high enough percentage of cases to have seriously influenced the results of the study. The proportion of patients who did not take all their pills also did not vary significantly between groups. Cross tabulations (not shown) of all these factors against subjective and objective improvement indicated that the elimination of patients who received supplementary medicaments or did not take all their pills would not have appreciably affected the results of the study.

Table 3 shows the effect of bioflavonoid and ascorbic acid on the improvement after three days, judged by both the patient and the clinician. The distributions with and without each of the drugs are almost identical, for both subjective and objective change, with absolutely no statistically significant differences demonstrable. This is graphically illustrated in figure 2. The ameliorating effects of the two drugs on the patients' symptoms are evaluated in table 4. It will be noted that on initial examination the percentage of patients in each group having each symptom was strictly comparable. The number of patients having the symptoms at the end of three days was then tabulated, and the percentage decrease, based on the number originally reported, was calculated. In a few instances patients developed symptoms after the first visit, but these cases were canceled by others in which the symptoms disappeared, and the number in any event was too small to affect the statistical significance of the data. The difference in percentage decrease that might be attributable to drug effect is shown in the right-hand column. It clearly indicates that neither bioflavonoid nor ascorbic acid had more than a random effect on any of the symptoms of the patients.

The effect of the two drugs on nasal secretions is shown in table 5. Again the initial distributions are well within random limits. There is a noticeable drop in the percentage with mucoid secretions after three days, but this change is almost identical in the groups receiving and not receiving both bioflavonoid and ascorbic acid. There is an actual increase in the per-

TABLE 5.—*Change in Nasal Secretions by Drug Groups*

Nasal Secretion	Initial No.	Initial %	Three Day No.	Three Day %	Change, %	Initial No.	Initial %	Three Day No.	Three Day %	Change, %
	With Flavonoid					Without Flavonoid				
None	281	30.3	462	49.9	+64.4	286	29.7	482	50.1	+68.5
Slight mucoid	442	47.7	297	32.1	−32.8	459	47.7	326	33.9	−29.0
Marked mucoid	142	15.3	85	9.2	−40.1	164	17.0	79	8.2	−51.8
Slight purulent	42	4.5	46	5.0	+ 9.5	27	2.8	34	3.5	+25.9
Marked purulent	19	2.1	36	3.9	+89.5	26	2.7	41	4.3	+57.7
Total	926		926			926		926		
	With Ascorbic Acid					Without Ascorbic Acid				
None	278	29.5	459	48.7	+65.1	289	30.6	485	51.3	+67.8
Slight mucoid	449	47.5	314	33.3	−29.9	453	47.9	309	32.7	−31.8
Marked mucoid	154	16.3	75	8.0	−51.3	152	16.1	89	9.4	−41.4
Slight purulent	35	3.7	44	4.7	+25.7	34	3.6	35	3.8	+ 3.9
Marked purulent	28	3.0	51	5.4	+82.1	17	1.8	28	2.8	+58.9
Total	943		943			945		945		

TABLE 6.—*Decrease in Nasal Obstruction by Drug Groups*

Nasal Obstruction	Initial		Three Day		Change, %	Initial		Three Day		Change, %
	No.	%	No.	%		No.	%	No.	%	
	With Flavonoid					Without Flavonoid				
None	570	59.7	705	73.9	+14.2	581	59.6	756	77.5	+17.9
Partial, one side	164	17.2	126	13.2	— 4.0	177	18.2	118	12.1	— 6.1
Partial, both sides	173	18.1	100	10.5	— 7.6	172	17.6	81	8.3	— 9.3
Complete, one side	19	2.0	9	0.9	— 1.1	17	1.7	6	0.6	— 1.1
Complete, both sides	28	2.9	14	1.5	— 1.4	28	2.9	14	1.4	— 1.5
Total	954		954			975		975		
	With Ascorbic Acid					Without Ascorbic Acid				
None	569	59.2	726	75.5	+16.3	582	60.1	735	75.9	+15.8
Partial, one side	171	17.8	124	12.9	— 4.9	170	17.6	120	12.4	— 5.2
Partial, both sides	170	17.7	84	8.7	— 9.0	173	18.1	97	10.0	— 8.1
Complete, one side	19	2.0	9	0.9	— 1.1	17	1.8	6	0.6	— 1.2
Complete, both sides	32	3.3	18	1.9	— 1.4	24	2.5	10	1.0	— 1.5
Total	961		961			966		968		

centage of patients having purulent nasal discharges, probably representing the development of secondary bacterial infection, but once more no significant effect on this phenomenon can be attributed to the drugs being tested. The changes in nasal obstruction in the course of the respiratory diseases are tabulated in table 6. The distribution by degree of obstruction was almost identical before treatment in the test groups. There was a uniform decrease in the amount of obstruction in all groups, with no significant differences attributable to either of the drugs.

In table 7, the amount and severity of the pharyngitis found is tabulated. Again there were no appreciable differences in the distributions before therapy. There was a uniform decrease in the amount of pharyngitis found after three days, with neither of the changes in distribution exhibiting more than random variation.

Although this study was designed for outpatient follow-up, it was felt that the disposition and lost time might shed some light on the function of the drugs. Table 8 indicates that there has been no effect on these factors. The proportion of subjects sent home from work on the first visit could not be attributed to drug effect, but the uniformity noted is another indication of the comparability of the groups with regard to severity of infection. The percentage sent home on a subsequent visit might be an inverse index of the efficacy of the medication, but again there was no appreciable variation. The mean number of days lost, which would be a function of both initial severity and drug effectiveness, also showed no statistically significant differences.

On the theory that the effect of the drugs on capillary permeability might only be beneficial if they were given at the start of the illness, the data on patients treated within 24 hours of the development of symptoms were sorted out and tabulated in table 9 for subjective and objective change after three days. Not only was no difference of effect noticed between the patients who did or did not receive either of the drugs, but the distribution by improvement did not differ significantly from that in the total number of patients, regardless of the number of days since onset (table 3).

Since the study was conducted in the dispensaries or offices under the supervision of three different physicians, it was considered advisable to evaluate some of the findings in each separately, to determine whether any had achieved significantly different results than the others. This analysis for subjective change is shown in table 10. It will be noted that the distributions are noticeably different under the three auspices, with statistical significance at well beyond the 0.1% level between all of them. This is due either to variation among the institutions in the standards for determining the subjective changes or to factors in the composition of the groups or the collateral treatment, such as the inclusion of students and private patients. The locality and the infecting organism may also be a factor. It is interesting, also, that all areas of the United States were included in this study. That it was not due to either bioflavonoid or ascorbic acid is evident from the fact that, despite wide variation in distribution between institutional groups, there were no statistically significant differences due

TABLE 7.—*Decrease in Pharyngitis by Drug Groups*

Pharyngitis	Initial		Three Day		Change, %	Initial		Three Day		Change, %
	No.	%	No.	%		No.	%	No.	%	
	With Flavonoid					Without Flavonoid				
None	530	57.7	703	76.6	+18.9	531	56.5	730	77.4	+21.1
Mild	302	32.9	175	19.1	—13.8	321	34.0	171	18.1	—15.9
Moderate	71	7.7	32	3.5	— 4.2	72	7.6	31	3.3	— 4.3
Severe	15	1.6	8	0.9	— 0.7	19	2.0	11	1.2	— 0.8
Total	918		918			943		943		
	With Ascorbic Acid					Without Ascorbic Acid				
None	520	57.0	721	77.6	+20.6	531	57.0	712	76.4	+19.4
Mild	318	34.9	167	18.0	—16.9	305	32.7	179	19.2	—13.5
Moderate	62	6.7	33	3.6	— 3.1	81	8.7	30	3.2	— 5.5
Severe	10	2.0	8	0.9	— 1.1	15	1.6	11	1.2	— 0.4
Total	929		929			932		932		

to the two drugs within any of the groups. The percentage differences noted, particularly in the Pratt-Whitney group, are still within the limits of random variation for a group of this size.

When the study had been running for several months, a preliminary check on the cases already reported indicated no effect from the bioflavonoids. On the off chance that another compound might prove more effective, the medicaments were switched from lemon to orange flavonoid and the study continued. The difference in effect of these two products on subjective and objective change is shown in table 11. While the lack of effect is more evident in the lemon flavonoid group, the differences noted between the patients receiving and not receiving orange flavonoid did not reach statistical significance and can be completely accounted for by chance variation. It will be noted that the results with orange flavonoid were significantly worse than those obtained with the lemon flavonoid controls. This difference is probably due to a change in the severity of respiratory disease in the later months when the orange compound was being evaluated and emphasizes the importance of simultaneous controls as were used in this study.

TABLE 8.—*Disposition of Cases and Mean Number of Work Days Lost by Drug Groups*

	Bioflavonoid				Ascorbic Acid			
	With		Without		With		Without	
Disposition of cases	No.	%	No.	%	No.	%	No.	%
Kept at work	860	87.4	854	87.3	854	88.4	860	86.3
Sent home after first visit	76	8.2	83	8.8	72	7.7	87	9.3
Sent home on subsequent visit	40	4.3	37	3.9	36	3.9	41	4.4
Total	922		944		932		934	
Mean no. of work days lost	1.171		1.305		1.091		1.384	

The lack of difference cannot be attributed to the limitation to a single reobservation. In any drug influencing the course of an acute self-limited disease, some changes must be noticeable in at least some of the symptoms after three days or else the effect is so negligible that it can be completely discounted. The procedure used did not evaluate the effectiveness of either of the drugs in preventing secondary bacterial infections and other complications, for which a minimum of a second reexamination after one week would have been necessary, because it had been designed to test the claim that the bioflavonoids, in conjunction with ascorbic acid, aborted or cured the common cold. Neither did it evaluate the use of these vitamins in prophylaxis against the common cold.

The study cannot be invalidated on the basis of too high a percentage of placebo reactors. It is well known that the majority of common colds are alleviated to some extent by the administration of any symptomatic therapy, and the improvement noted in the over 1,900 cases is about what one would expect after three days of such therapy. For the claims for the drugs being tested to be substantiated, there would have to have been present an effect over and above that found for the entire group, and this difference was completely lacking.

It will be noted that no analyses were performed on the individual drug groups to evaluate synergism or antagonism. In the absence of any differences between the combined groups specific for bioflavonoid and for ascorbic acid (see section on methodology),

TABLE 9.—*Subjective and Objective Change in Patients Treated in First Twenty-four Hours by Drug Groups*

	Flavonoid				Ascorbic Acid			
	With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%
Subjective								
Worse	65	11.2	61	11.5	62	11.1	64	11.6
None	125	21.6	113	21.3	122	21.8	116	21.1
Improved	241	41.6	215	40.5	236	42.1	220	40.0
Cured	148	25.6	142	26.7	140	25.0	150	27.3
Total	579		531		560		550	
Objective								
Worse	41	7.4	49	9.4	46	8.5	44	8.2
None	112	20.1	87	16.7	100	18.4	99	18.5
Improved	255	45.4	239	45.8	254	46.7	238	44.5
Cured	171	27.1	147	28.2	144	26.5	154	28.8
Total	557		522		544		535	

TABLE 10.—*Subjective Change by Study Groups*

	Tebrock				Arminio				Johnston			
	With		Without		With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Flavonoid												
Worse	91	12.7	102	13.9	0	0	1	0.9	21	17.6	15	12.3
None	155	21.6	145	19.6	35	32.1	29	25.4	30	25.2	42	37.2
Improved	307	42.8	303	40.9	46	42.2	54	47.4	54	45.4	44	38.9
Cured	165	23.0	190	25.6	28	25.7	30	26.3	14	11.8	12	10.6
Total	718		741		109		114		119		113	
Ascorbic Acid												
Worse	90	12.7	101	13.9	0	0	1	0.9	15	12.9	21	18.1
None	143	19.6	137	21.5	35	32.1	29	25.4	47	40.5	25	21.6
Improved	322	44.1	288	39.5	47	43.1	53	46.5	41	35.3	57	49.1
Cured	172	23.6	183	25.1	27	24.8	31	27.2	13	11.2	13	11.2
Total	730		729		109		114		116		116	

Comment

The overwhelming impression gained from all these data is the singular lack of effect produced by either the bioflavonoid or the ascorbic acid. If any real clinical response were produced by either of these drugs in even an appreciable minority of the patients treated with them, significant statistical differences should have been evident in at least some of the factors observed. This is particularly so because of the large sample size and the exact comparability of the test groups for all observed factors at the start.

it seemed necessary to look for such effects. It is statistically possible for two drugs to both have a beneficial effect but to be completely antagonistic and cancel each other, in which case the analysis used would yield a false-negative result. An unusual effect

TABLE 11.—*Difference Between Lemon and Orange Flavonoid*

	Lemon				Orange			
	With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%
Subjective								
Worse	102	12.6	101	12.3	10	7.4	18	12.1
None	171	21.1	157	19.2	49	36.3	59	39.6
Improved	338	43.5	342	41.8	54	40.0	59	39.6
Cured	186	22.8	219	26.7	22	16.3	13	8.7
Total	811		819		135		149	
Objective								
Worse	68	8.8	72	9.0	5	3.8	15	10.3
None	134	19.8	145	18.1	41	31.1	39	26.7
Improved	369	47.5	368	45.9	60	45.5	75	51.4
Cured	186	23.9	216	27.0	26	19.7	17	11.6
Total	777		801		132		146	

of this kind, however, would be immediately apparent by simple inspection of the data at the time the groups were combined, and it was not noted.

Thus far there is no convincing evidence that bioflavonoids or ascorbic acid can alleviate a cold when used alone or in combination with other therapies, and our evidence confirms the conviction that bioflavonoids or ascorbic acid are without specific effect in such conditions. Although some might argue that much higher doses of either bioflavonoids or ascorbic acid are necessary to demonstrate a curative effect, we emphasize that the patients in this study received 200 mg. of ascorbic acid and 1 gm. of bioflavonoid per day, levels generally considered adequate to affect the capillary permeability. Since the usefulness of these compounds in reducing capillary fragility has generally been applied to long-standing conditions, there is no reason to believe that massive doses would achieve the rapid effect necessary in conditions as acute as a cold.

Summary

The effect of 1 gm. of bioflavonoid and/or 200 mg. of ascorbic acid administered daily in aborting or curing the common cold was tested in a controlled double-blind trial on over 1,900 subjects. The medicaments were given, either singly or in combination, in addition to the usual treatment used to alleviate symptoms. No appreciable effects were observed after three days on subjective or objective improvement; on disappearance of running nose, sneezing, cough, hoarseness, malaise, headache, postnasal drip, or sore throat; on decrease in nasal secretions or obstruction or pharyngitis; or in time lost from work. In our opinion neither of these drugs in the dosage given has any significant effect in altering the course of the common cold.

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The following doctors from the staff of Sylvania Electric Products, Inc., recorded and commented on the clinical observations used in this study: William Young, Hilton Lopez, Manuel Kaufman, Thomas Foote, C. Stafford Clay, William H. Regelman, Russell Pfeil, Jerome Paparella, Charles Youngman, S. C. Bower, George Means, S. Gardner, Edwin Reynolds, Cornelius Driscoll, Emil Bove, Charles Fleck, Paul Gallaher, Carl Lohmann, Joseph Zavisca, George Cody, and Quay McCune.

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CLINICAL NOTES

A SIMPLE AID IN CALCULATION OF DIETS

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In the construction of diets for alteration of the body weight of adults, certain assumptions have long been employed. Though not entirely accurate, they have the merit of utility and may be stated briefly as follows: 1. For every individual there exists an "ideal" body weight, which may be calculated by a rule of 110 lb. (49.9 kg.) for a person 5 ft. (152.4 cm.) tall, with 5 lb. (2.3 kg.) added for each additional inch. It is customary to allow a variation of 10% in this value, depending on body build. 2. A person who is mainly sedentary requires a daily dietary allowance of 35 calories per kilogram of body weight. If he eats 35 calories per kilogram of his ideal weight, his actual weight, regardless of what it is, will remain constant. If he does heavy labor, however, his caloric requirement may be as high as 40 or 50 calories per kilogram per day. 3. If a person eats more than 35 calories per kilogram of his ideal weight per day, he will gain weight at the rate of 1 gm. of fat plus 1 gm. of water for each 9 calories in excess. If he eats less than the ideal amount, he will lose correspondingly.

These assumptions, admittedly only approximately correct, may be used for calculating weight-changing diets, as in this example. An office worker who is 5ft. 6 in. (167.6 cm.) tall wishes to lose 11 lb. (5.0 kg.) in a month. The required diet is found from the following computations: (1) 11 lb. = 5 kg. = 5,000 gm.; (2) 5,000 gm. ÷ 30 days = 166 gm. per day, equivalent to 83 gm. of fat plus 83 gm. of water per day; (3) 83 gm. of fat is the equivalent of 83 × 9, or 747 calories less

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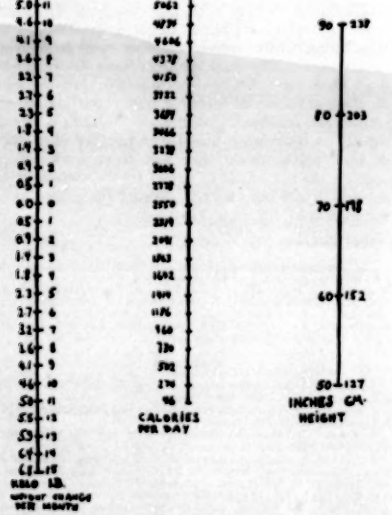
than the ideal diet per day to lose 11 lb. in one month; (4) the ideal weight is 110 lb. for the first 5 ft., plus 30 lb. for the additional 6 in. This 140 lb. is approximately 64 kg. At 35 calories per kilogram of body weight, the "ideal" diet is 35 × 64, or 2,240 calories per day; and (5) deducting the required amount (2,240 − 747) gives 1,493, or roughly 1,500 calories per day to produce the desired rate of weight reduction.



Nomogram for calculation of weight-changing diets. Select the patient's height along the right margin and the rate of weight loss or gain desired per month along the left margin. The line connecting these two points crosses the caloric line at the desired daily caloric allowance.

While this type of calculation is simple, it is rather time-consuming. The method can be reduced as follows to a general equation that will cover all cases of moderately sedentary adults. Let H = height in inches, L = pounds per month weight loss (or gain) desired, and C = calories per day. Then, the ideal weight is 5(H − 60) + 110, and the ideal diet in calories per day is

$$35\left[\frac{5(H-60)+110}{2.2}\right].$$

The pounds of fat and of water lost per day are converted to calories lost per day by the term

$$\frac{L\times 9\times 1{,}000}{2.2\times 2\times 30}.$$

The difference between these two terms gives the required number of calories:

$$C=35\left[\frac{5(H-60)+110}{2.2}\right]-\frac{L\times 9\times 1{,}000}{2.2\times 2\times 30}.$$

This may be further simplified to

$$C=11.4\,(7H-266-6L).$$

Yet another saving of time and effort may be introduced by constructing a nomogram based on this general equation, by which caloric allowances may be selected at a glance for any desired weight change. Such a nomogram is shown in the figure, based on a standard requirement of 35 calories per kilogram of body weight.

230 N. Broad St., Philadelphia (2).

RAPID ESTIMATION OF BLOOD GLUCOSE CONCENTRATION WITH ORDINARY TES-TAPE

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An instantly available diagnostic aid and therapeutic guide for the rapid estimation of blood glucose concentration has been conspicuous by its absence. Previous attempts to meet this need by streamlining the usual time-consuming laboratory procedure have included those of Wilkerson and Heftmann [1] and Leech and Woodford,[2] as well as the use of Dextrotest, a simplified blood sugar test outfit. These attempts have not met widespread acceptance because they require special equipment that is cumbersome to operate. An indicator paper known as Tes-Tape is now being increasingly used by patients with diabetes for the detection of urinary glucose. The green-blue spectrum appearing on the yellow Tes-Tape is indicative of the presence of glucose, since the color development depends upon the oxidation of glucose by its specific enzyme, glucose oxidase.[3] The advent of Tes-Tape has enabled development of a rapid and simple means for approximating the blood glucose level. By the method to be described, within three minutes after venipuncture severe hypoglycemia or frank hyperglycemia can be distinguished from an essentially normal blood sugar level. Within another few minutes the blood glucose value can be bracketed with an accuracy varying from 25 mg. per 100 cc. at very low concentrations to 200-250 mg. per 100 cc. at high concentrations of blood sugar.

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Materials and Methods

Determinations of glucose in whole blood and plasma were performed in duplicate on 130 specimens of oxalated venous blood by the "true blood sugar" method.[4] The glucose content of each sample of plasma was

simultaneously estimated with Tes-Tape by two different techniques. The first method involved the use of undiluted plasma. One drop of plasma was placed on one end of a strip of Tes-Tape about 1.5 in. in length. Sixty seconds later the darkest color that had developed was compared with the Tes-Tape color card and read on a scale with gradings from "4+" down to "trace" or "faint trace."

The second method involved the use of serial dilutions of plasma. When hyperglycemia was anticipated or when the approximate blood sugar level was unknown, eight small test tubes (e. g., Kahn tubes) were placed in a test-tube rack. Plasma was put into an end tube, and 10 drops of distilled water were added by medicine dropper to each of the other tubes. Ten drops of plasma were mixed with the water in the second tube, and serial dilutions from 0 to 1:128 were obtained. Correspondingly fewer dilutions were made if a normal or low glucose concentration was expected. Eight strips of Tes-Tape about 1.5 in. long were then placed side-by-side on a white paper background. To one end of each strip a single drop of a successive dilution was applied. The "end-point" was that dilution of plasma showing at one minute the last definite greenish tint on the yellow Tes-Tape. The end-point was usually sharp, but comparison with a blank—a strip of Tes-Tape moistened with water—occasionally facilitated decision regarding the last positive dilution. Figure 1 shows the results of the testing by this method of two samples of plasma for which the corresponding blood sugar levels were 93 and 311 mg. per 100 cc.

Results

Blood glucose concentrations of the 130 specimens ranged from 16 to 760 mg. per 100 cc. With few exceptions their corresponding plasma glucose values were slightly higher. The absolute increase of plasma over blood sugar levels varied from −7 to 88 mg. per 100 cc. (mean of 12 mg. per 100 cc.), with the greatest increments accompanying the highest blood glucose concentrations. In all instances blood and plasma values correlated so closely that the Tes-Tape response to plasma glucose reflected the corresponding blood glucose level.

The degree of glycemia could be quickly estimated by use of either of two indexes. A very rapid approximation was provided by the Tes-Tape reaction to undiluted plasma alone. Figure 2 illustrates that, despite considerable overlapping of the color readings for a given blood sugar value, the following interpretations of clinical utility were obtainable: 1. No color or the faintest green tint (faint trace) was evidence of severe hypoglycemia. 2. A pale green of variable intensity (trace to 1+) embraced a wide spectrum extending from very low to moderately elevated blood sugar values. 3. A deep-green color alone (2+) or one merging into blue (3+) signified progressive degrees of hyperglycemia. One factor contributing to the grossness of the interpretation from undiluted plasma was the frequent difficulty in deciding between trace and 1+ or between 2+ and 3+ readings.

Precision in estimating the blood sugar concentration was sharpened considerably by determination of the end-point, as described, for serial dilutions of plasma. Figure 3 demonstrates that the dilution technique permitted much better discrimination between hypoglycemia and normoglycemia. Degrees of hyperglycemia were also distinguished more exactly when the weakest dilution to show a color change on Tes-Tape was read. Not infrequently, however, it was still impossible to differentiate normal fasting blood sugar values from moderately elevated ones. The table is derived from the graphic data shown in figure 3. At each dilution of plasma recorded as the end-point, 90% or more of the corresponding blood glucose values fell within the range indicated. The glucose content of a specimen whose Tes-Tape response ended at or before the 1:2 dilution was alarmingly low, and an end-point at 1:4 still signified clinically important hypoglycemia in most cases. On the whole, the 1:8 dilution end-point indicated either slightly subnormal or normal sugar concentrations. At the 1:16 dilution the corresponding blood sugar value was either in the normal fasting range or moderately high. Positive responses at succeeding dilutions uniformly meant proportionately elevated glucose levels.

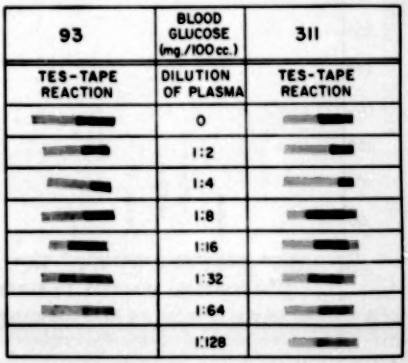

Fig. 1.—Tes-Tape indexes of two samples of plasma for which corresponding blood glucose concentrations are 93 and 311 mg. per 100 cc. On left, undiluted plasma shows 1+ reaction and last positive dilution is 1:16; on right, respective readings are 2+ to 3+ and 1:32. Two lower strips in each column show slight shadow cast by negative dilutions.

Comment

Depending upon the clinical information desired, the very rapid answer obtained from the Tes-Tape reaction to undiluted plasma may provide sufficient information to render a further plasma-dilution test unnecessary. For example, extreme hypoglycemia and severe hyperglycemia are instantly apparent. However, since the gradation between readings of trace and 1+ or 2+ and 3+ is often indistinct, the much closer approximation made possible by the serial-dilution technique more than compensates for the small additional investment of time.

During the development of the method, certain practical points of procedure became evident, recognition of which should facilitate duplication of the results reported: 1. Only one drop of plasma or its dilution should be placed on the Tes-Tape strip. There should be enough liquid to permit a slowly advancing fluid front during the minute of color development, but a dry area must remain at the time of reading, as shown in figure 1. If the strip is flooded, the excess of glucose-containing solution leads to overreading of the end-point by one or more dilutions. 2. The reading should be made promptly at from 60 to 75 seconds. Not only do some negative dilutions develop a greenish tint after 90 seconds but a blank of Tes-Tape moistened with water sometimes shows a similar color change after a few minutes. Apparently, the indicator color in the Tes-Tape system is activated minimally and nonspecifically by water per se. 3. There are no false-positive readings, since the enzyme upon which color development depends reacts specifically with glucose.[3] Neither the slight hemolysis sometimes present in plasma nor coexistent high blood levels of fructose interfere with the Tes-Tape response to the glucose concentration.

The rapidity with which this simple procedure informs the physician of the approximate blood sugar level of his patient makes it a useful adjunct in several clinical situations. In the emergency room, hypoglycemic coma can be quickly distinguished from other forms of unconsciousness. In the former case, the Tes-Tape will show at best a faint green reaction to the undiluted plasma and be negative beyond the 1:2 dilution, whereas for patients in any other state it will yield a positive response past the 1:4 dilution. On the diabetic ward of the hospital occasions frequently arise when one suspects that a patient may be hypoglycemic. Although the Tes-Tape color response is not keen enough to distinguish mild hypoglycemia from low-normal glucose values, it can easily single out a patient whose symptoms may well be due to hypoglycemia from those with obviously normal or elevated blood sugar levels. The Tes-Tape procedure can also be used conjointly with the method of Duncan and Gill[4] for estimating plasma acetone levels in order to follow the clinical course of a patient in diabetic coma. In the latter test, the diminishing intensity of color change produced by serial dilutions of plasma on the nitroprusside reagent heralds the disappearance of ketosis and a rising carbon dioxide–combining power. Similarly, a falling blood glucose level is signaled by a progressive decrease in the plasma dilution causing the last greenish tint to appear on Tes-Tape.

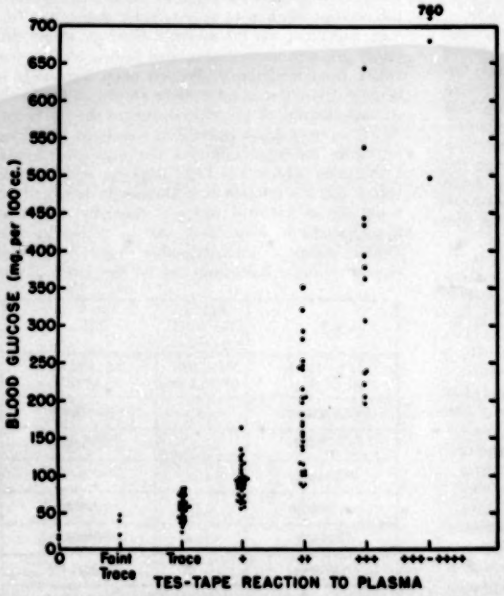

Fig. 2.—Correlation of blood glucose level with Tes-Tape reaction to undiluted plasma. Extreme hypoglycemia and frank hyperglycemia are recognizable, but grossness of reading index prevents good discrimination at intermediate sugar concentrations.

In addition to the above obvious applications of Tes-Tape, it may also prove useful in the screening of specimens of blood during diabetes-detection programs. The simplicity of the technique overshadows the fact that the Tes-Tape response is slightly less precise than that of the Wilkerson-Heftmann method,[1] the use of which is limited to a few diagnostic centers because of the special equipment and training required. Moreover, once plasma has been separated from red blood cells, the glucose concentration remains virtually unchanged for 48 hours or longer, so that a multitude of samples can be collected and screened en masse. On undiluted plasma, a Tes-Tape response of 3+ would automatically make the donor suspect, and a 2+ reaction would warrant further investigation if serial dilutions remained positive at 1:32 or higher.

Correlation of End-Points of Tes-Tape Response with 90% or More of Corresponding Blood Glucose Concentrations

Dilution of Plasma	Blood Glucose Values, Range of Mg./100 Cc.
0	15-20
1:2	20-40
1:4	35-65
1:8	65-95
1:16	75-165
1:32	145-265
1:64	225-450
1:128	500-700

A final word about the probable future of this test relative to its present status: It is almost certain that we shall ultimately see the development of vastly improved paper indicator systems whereby direct, instantaneous, and highly accurate assessment of the

plasma glucose level will be possible. When that happens, ordinary Tes-Tape will become as obsolete as litmus paper. In the meantime, however, the comparatively gross information provided by the method described does not discredit its general applicability today. Here, for the first time, by the use of a "litmus-paper" technique and a material that is available in all pharmacies, valuable information can be quickly obtained regarding the blood sugar concentration of the patient.

Summary and Conclusions

A simple technique, based upon the color response of ordinary Tes-Tape to plasma, enables rapid gross estimation of the blood glucose concentration. Either severe hypoglycemia or frank hyperglycemia can be instantly distinguished from normal blood sugar values by observing the Tes-Tape reaction to undiluted plasma. More precise information is obtained by determining the color response to serial dilutions of plasma. This procedure offers a range of accuracy that is proportional to the actual level of glucose in the blood. At glucose concentrations that are below 50 mg. per 100 cc. one can usually read within 20 to 30 mg. per 100 cc., while at very high levels the reading range widens to 200 to 250 mg. per 100 cc. The simplicity and rapidity of the test and the availability of materials recommend the test for general use whenever prompt information regarding the patient's approximate blood sugar level is desired.

4500 S. Lancaster Rd. (2).

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The Tes-Tape used in this study was supplied by Mr. Walter H. Stein of Eli Lilly & Company, Indianapolis.

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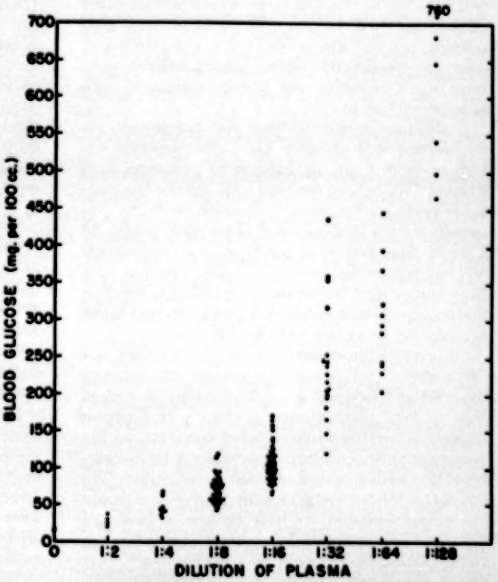

Fig. 3.—Correlation of blood glucose level with end-point Tes-Tape response to serial dilutions of plasma. Degrees of hypoglycemia and hyperglycemia are satisfactorily interpreted. Normal sugar values may or may not be distinguishable from moderately elevated ones.

MEDICINE AT WORK

THE DOCTORS WHO TALK ABOUT WAR

Around a green baize-covered U-shaped table in Washington, D. C., two dozen doctors were talking about a war they hope never will come. What they heard and said might some day affect not only physicians but all Americans in every walk of life. Here, published for the first time, are elements of that story as it was unfolded last Oct. 25 by representatives of a dozen federal agencies at the meeting of the Committee on Civil Defense, Council on National Defense, of the American Medical Association.

News Item

The U. S. Federal Civil Defense Administration revealed that the government now is completing a prototype of a plastic "basic protective mask" in six shapes and sizes for possible civilian use against chemical warfare. Dr. John M. Whitney, who is director of the health office of the FCDA, told the committee that if and when the government decides there should be mass distribution of the masks, the FCDA simply will rush sets of master molds to manufacturers across the country. The factories then can produce the masks quickly by a plastic injection method. Until now, the FCDA had considered air pollutant defense secondary to nuclear war effects.

Dr. Whitney also announced that medical supplies for three and a half million casualties over a three-week period now are stored in 40 warehouses across the United States and that by 1958 the cache will be big enough for five million victims of any national catastrophe.

News Item

The Atomic Energy Commission's long-awaited new handbook on the effects of nuclear weapons is now in final proof and will be available for distribution in a few months. Robert L. Corsbie of the AEC's division of biology and medicine says the handbook will be in less technical language than a now-outdated edition, and "will be accessible to many more non-scientific people." The publication is expected to answer, for the general public, many persistent questions about radiation and biology associated with H-bomb explosions.

It also may answer criticism that the present administration in Washington has tried to suppress disturbing reports on the dangers of radiation. Said Corsbie: "We believe now that although the law justifiably keeps nuclear devices classified (as secret), information from field tests should be made public. As a result, three-fourths of our 47 weapons test reports will be made available soon." Corsbie, who was on a Navy survey team at Hiroshima in 1945, also revealed that an important re-survey of A-bomb effects in Japan is producing some new and valuable data.

For example, a medical survey team 10 years ago "documented" the case of 100 persons who survived the blast at Hiroshima by seeking shelter in a cave. But last year another team, working with Japanese physicians, carefully reconstructed conditions at the same cave and found that the refugees actually numbered 67, of whom only 2 survived. Says Corsbie: "We feel that if we are wrong on early findings, we should say so. For example, we have thrown out a theory that blast and radiation burns occur only when the victim is in open-line sight of a nuclear blast. That theory was disproven when the explosion of a 15-kiloton device from a 300-foot tower caused burns around the eyes and groin of dogs which were 1,500 feet away in a shelter built with two right-angle turns."

News Item

A nationwide network of "revitalizing" teams is being organized by the U. S. Air Force to speedily restore combat crews into retaliatory shape in case they are hit by an enemy attack. Air Force Col. Joseph Nagle announced that by 1958 eight of these 118-man "casualty management and control" units will be set up near (but not in) Strategic Air Command base areas. He says: "If as a result of these units we can launch one more B-52, they will have paid for themselves." Civilians would not be served by these Air Force units. They would have to "shift for themselves" through their local civil defense organizations and would, in fact, be expected to give medical aid to the military (instead of vice versa) during the early stages of an enemy attack.

Other News

Other news was occurring in that hotel meeting room—news about expanded civil defense training for public health reservists, about a nationwide survey of community water systems, about a few AEC advances against radioactive fallout, and about continuing government research on the effects of nuclear explosions and of biological and chemical warfare contaminants on foods and drugs.

Dr. Harvey Stone of the health resources advisory committee of the Office of Defense Mobilization told the physicians that, to his great surprise, he learned that a single nuclear bomb could wipe out all three U. S. firms that manufacture surgical instruments. Almost the same geographical proximity is true of x-ray equipment companies in this country, he said. It was something to think about.

And there was something else to think about: In case of enemy attack, where does a physician's responsibility lie? Does he rush to duty at his hospital or does he rush into uniform from reserve status? Is

Left, civilian protective mask being developed for possible mass use against chemical warfare. The Federal Civil Defense Administration says that the mask—designed in six variations of shapes and sizes—can be produced in local factories by a plastic injection method. The FCDA would keep the master molds.

Middle, Los Angeles—American Red Cross demonstration of what an "emergency disaster" would be like. Although it was not said, this could have been a cross section of the aftermath of an A-bombing. Realism was added by administration of blood plasma to "victims."

Right, in Flint, Mich., June 11, 1953, "Tornado's Toll," injured residents of Flint lined row on row in the gymnasium of the wrecked school, after the emergency shelter was set up to meet the need of treating injured and homeless when hospitals in the area became packed with casualties. More than 125 persons were killed and many hundreds injured in the violent twister.

it his prime obligation to fulfill key duties in his state civil defense organization, or at the nearby first-aid station—or at the stricken factory where he may have been employed part-time? For many physicians, it can be a multi-responsibility beyond their priority control.

Already, the ODM has a special task force working on the problem. The A. M. A. Committee Chairman, Dr. Harold Leuth, suggested to his colleagues: "The matter of a doctor's dual responsibility is a top cabinet decision in our government." This doctors' dilemma has not yet been resolved; it still is being considered.

Members also are considering the stark contrast of civil defense in this country and in Great Britain. They heard U. S. Army Col. Joseph R. Schaeffer, recently returned from three days in England, say: "The British are very alert to disaster situations. They continually are exercising for atomic war. I saw one man who travelled 200 miles to London at his own expense—just so he could lie in the rubble of a street, as a casualty model wearing realistic-looking wounds. He was observed and worked over by students, passersby, even members of Parliament—all of whom were eager to learn what they could do to help themselves in a disaster. There is nothing like it done in this country. In the extreme apathy in the United States, many of us are geared to believe it won't happen."

Doctors Are the Pathfinders

Nothing like it in this country? A committee member, Dr. Carroll Hungate, questions that. Admittedly, many states have fallen down on civil defense, he said, but others—including California, New York, and Kansas—are pretty well prepared. Dr. Hungate cited a recent exercise in Stanley, Kan., where nonmedical people cared for simulated casualties, and evacuated their entire town to a school house 35 miles away. He said: "In many states doctors have been and are stimulating other people and agencies into civil defense activities. They were in civil defense long before others were." Said another committee member, Dr. Cortez F. Enloe Jr.:

"From the moment the first attack warning comes, something you're doing will be affected by the civil defense measures now planned. This holds true whether you are practicing pediatrics in Paducah or plastic surgery in Manhattan. . . . The ultimate success of the national civil defense program and of the programs of the American Medical Association, of the state, and of county medical societies depends, in the final analysis, not on what authorities think and plan but on what the individual physician does. . . . For the physician, civil defense is a personal matter."

It was an immediate personal matter for hundreds of northern California physicians last Christmas when they put aside holiday plans in order to implement their own long-standing civil defense plans—and thus helped reduce the toll of human life during ravaging floods. It was an immediate personal matter for hundreds more, including 42 public health reservists called to active duty, during last year's New England floods. It was an immediate personal matter for the county medical society members in Fremont, Mich., as they took up the grim task of sorting casualties from a devastating one-two punch delivered by twin tornadoes. Wherever there has been natural disaster, it was the prearranged civil defense blueprint of local medical societies that served the community. And it was during these same disasters that the societies without civil defense training saw higher casualty figures; comparative records across the country prove that.

How to instill civil defense unity without uniformity among this nation's medical men is a major objective of the A. M. A. Committee. One suggestion being considered is the formation of a "national medical board" made up of one doctor from each state medical organization, which would offer ideas for survival. These locally applicable ideas then could be transformed democratically into specific standards and training duties, extending to the county level. As a result, doctors then might be able to do more than just vaguely "help" in their community's civil defense.

Simple geometrics makes it plain that the physician's role in a community disaster is multiplied a thousandfold when a catastrophe strikes the nation. The doctors themselves clearly defined their mission last June when their A. M. A. House of Delegates overwhelmingly voted approval of a national civil defense resolution stating:

"It is therefore the solemn duty of the medical profession, including every individual physician in the country, to exercise his skills, knowledge and best judgment to prevent human suffering and loss of life and to assume responsibility for solution of the complex medical problems arising from instantaneously produced mass casualties."

Pancreatic Insufficiency.—A number of children with cystic fibrosis of the pancreas with complete pancreatic enzyme deficiency as well as a number of healthy children were studied to determine whether the response of their plasma proline levels to the feeding of either gelatin or casein could be used as a simpler and more generally useful diagnostic test. A new simple method for the determination of plasma proline has been found suitable, and its application indicates that it can be used in conjunction with or that it may replace the glycine method. The proline method has the advantage that it may be applied after casein or gelatin meals, whereas the glycine method is useful only after gelatin meals. Children with cystic fibrosis of the pancreas with complete pancreatic insufficiency have a fasting proline plasma level much below that of healthy children, whereas the fasting aminoacetic acid levels are approximately the same. The administration of a proteolytic enzyme preparation, papain, with the test meal of gelatin to patients with pancreatic insufficiency results in a significant improvement in protein digestion.—B. S. Gould, Ph.D., and H. Shwachman, M.D., Studies in Cystic Fibrosis, *A. M. A. Journal of Diseases of Children*, June 1956.

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TRAINING OF THE FAMILY DOCTOR

GUEST EDITORIAL

Charles S. Davidson, M.D.

"Everyone wants and should have a family doctor." "This is the age of specialization." "Generalists are our family doctors of the future." "Someday we'll have a doctor for every part of us." "You don't get the personal medical care you used to." "The internist is the general practitioner of today." "We must consider the patient as a whole." These statements and many others are from physicians, editors, and lay people. Their variety and very number demonstrate that something is afoot. True—and it is just this: The complexity of modern medicine demands specialists; yet each of us when ill wants a doctor who understands us and will "see us through," who will consider the social, economic, and emotional problems as well as the pain. We might like our family doctor to take care of our glioma, yet we know that a neurosurgeon can do it better. This dichotomy between family doctor and specialist runs throughout medical practice and has given rise to the clichés above as well as to much heated discussion. Part of the heat of the discussion arises from lack of proper definition of a few words.

Let us use the term family doctor for one whom we call first when we are ill, to whom we go for "health examinations"—a physician who knows us as thoroughly as anyone can. Now who is best trained to do this, to be our family physician? Some say the generalist (general practitioner), who is (theoretically) qualified to some extent in all aspects of medicine; some say the internist; and some hope that every physician (including the neurosurgeon above) is capable of such complete medical care.

When we choose a family doctor we want to know not only about his intellectual and moral qualifications but also about his training and experience. Assume that a young man is about to graduate from medical school and wants to be a family doctor. Assume also that he has a fine mind, is morally sound, likes people, and will "make a fine doctor." What advice should he be given for his further training? He does not wish to specialize in surgery, obstetrics, neurology, or psychiatry but wants to be a good doctor. My thesis and my advice to the young man follows. No one can do major surgery, specialized surgery, obstetrics, gynecology, and psychiatry without extensive training in each subject. A person who may do all or most of these and do them well should have, after internship, intensive training and experience for at least four or five years after medical school. He is then qualified to start general practice as defined above. One year of rotating internship today is not enough to permit him to undertake all these things and do them well. In fact, general practice, as I see it, requires more years of intensive training than do many specialties. That this is beginning to be recognized is implied by the formation of general practice residencies by some hospitals. Whether many persons can afford the years of training necessary to become well-trained generalists may be doubted.

If our young man does not want to or is not able to spend this time but still does not want to be a specialist, what is he to do? I would recommend that he spend two or perhaps three years in hard hospital work, much of it in general medicine. During this time he will have worked with specialists such as surgeons, pediatricians, obstetricians, and psychiatrists and will have learned much about the problems with which they are dealing. He will thus be trained to be a family physician—not to do major surgery and probably not obstetrics, unless necessary in his community (and then he will take training), and perhaps will need to refer some or all children's problems to his colleagues in pediatrics. But he is trained to care for everyday problems and illnesses in the family. Perhaps he may wish to specialize in internal medicine, even in one of its subspecialities, and may become qualified for admission to and be certified by the American Board of Internal Medicine, but this is by no means necessary to nor usually advisable for his training as a family doctor. Parenthetically, many internists are family physicians today. As the physician grows older and becomes more widely experienced, consultation practice may fall his lot. Just as likely, and in spite of experience and even "boards," he may be happier and be of greater service continuing as a family doctor, calling on others with specialized training when necessary.

Whatever the course of his professional career, our young man will be sufficiently well trained never to undertake that for which he is not qualified. In this "age of specialization," the practice of medicine will continue in its best tradition if each physician does only that which he is capable of doing well, irrespective of postgraduate diplomas and recognition by specialty boards and other approving authorities, for these latter are only gross "paper" standards. A physician's knowledge of his capabilities and his own conscience are far better standards for his conduct as a physician and as to the kind of practice he will undertake than the titles others may give him on the basis of credentials, examinations, and years of residency training. To illustrate: If our young man, after four years of medical school and one of rotating internship, assays to practice medicine, sur-

From Thorndike Memorial Laboratory, Boston City Hospital.

gery, and obstetrics, he is fooling not only himself but his patients. So also is the expert neurosurgeon who, unaided, treats diabetes, hypertension, and the occasional obstetric case.

Let us then redefine the kinds of physicians in modern terms and say that the general practitioner will need sufficient training (four or more years after medical school) to permit him to practice medicine, surgery, obstetrics, and other specialties. The family doctor who "knows us best" and "sees us through" as far as his training and capabilities will allow may be such a general practitioner, or, more likely, he will have had far less training—the majority of it in medicine. The specialist has the kind of mind and the training to dig deep into a particular field—be it orthopedic surgery, psychiatry, or cardiology—and probably will have neither the time nor the inclination to be a family doctor, although this does not imply that he is any less a physician in the best sense of the word. We must do well that for which we are trained, but only that of which we are capable.

MEDICINE AND THE ARMED FORCES

Physicians about to perform their military obligation for the first time, their colleagues now in service, and those who have already served would have felt quite encouraged had they witnessed the recent meeting of the Committee on Military Medical Affairs of the American Medical Association. This group, which is a part of the A. M. A.'s Council on National Defense, meets at least twice a year with the expressed hope of securing the optimal interests of the medical and allied professions to serve the nation, compatible with national defense needs. By invitation, this particular committee assists the armed forces in matters of planning for medical care, physician recruitment, reserve programs, military medical supplies, deferment policies, and many other fields where medicine and the military have a joint interest. In addition, this A. M. A. activity carefully investigates complaints, as well as accolades, from physicians who, because of present or past military duties, have written and elaborated on what appear to be either professional injustices or excellent examples of military medicine in action.

The most recent meeting of the Committee was held in Washington, D. C., this past October. Representatives (in most cases the surgeon general, along with members of his staff) of all the armed forces, the Public Health Service, the Selective Service System, and the office of the Secretary of Defense volunteered their time to discuss with the Committee items that would involve a physician and his relation to military medicine. A few of these subjects might serve to illustrate the Committee's activities.

Prime interest was of course centered around the "doctor-draft." Recent newspaper publicity has intimated that the Defense Department is not planning to ask for a continuation of this legislation. The A. M. A. representatives were interested in any future plans for the possible call-up of practicing physicians. Government spokesmen agreed on the diminishing justification of their previous viewpoints concerning this special registration and went on to explain their present concepts for maintaining an adequate number of physicians to care for military personnel. First, they plan to ask amendment of the present regular selective service act to place physicians in the same category as all other specialists occasionally needed to provide optimum security for national defense. Second, initial reports on the Career Incentive Program for Medical Officers (Public Law 497, 84th Congress) seem to indicate an increasing interest in a military medical career, with greater numbers of applications for commissions being submitted and, at the same time, fewer resignations of medical officers. In projecting their needs after June, 1957, based on the continuance of the *status quo* or on improvement in world affairs, the military felt that, by its use of physicians who would have come under the regular draft but who had been deferred to complete their education, in addition to increasing numbers of volunteers, there would be adequate and competent medical care for members of the armed forces.

Military reserve activities were fully explained to the Committee by all the services represented. New programs for reservists, with special emphasis on the potential benefits to the physician becoming a member of a reserve component in his home area, were graphically demonstrated. The Committee requested that all new reserve information be compiled in an easily readable form and published for the information of the profession.

Discussion was also held concerning the dual, or in some cases triple, responsibility of the medical reservist. Specifically, there is the situation of the reserve officer presently in government employ, as in a Veterans Administration hospital. In the event of a state of emergency, which organization has prime call on the man? In a situation where a physician or nurse is a member of a reserve component and holds a key position of supervision in a medical or teaching center, does he or she owe first allegiance to the branch of the armed forces, the affiliated institution, or to community civil defense? The A. M. A. representatives felt this was an urgent problem worthy of further detailed study and secured the assurance of the military medical chiefs not only that such investigation of the government employee–reservist was now in progress but that consideration of the priority of the nongovernment reservist would also be undertaken.

Another of the many matters explored pertained to the new Central Medical Material Supply Program. The responsibility for this particular program is now vested in the Department of the Navy for all three military services. There was an informative exchange of information and ideas, based on past war and peacetime experiences along with projected possibilities, the central theme developed being to provide the most efficient supply service when and where needed, while still maintaining the desired economy of operations.

The cooperative attitude of the military officials in working with the members of the Committee on Military Medical Affairs reflected a sincere desire to work hand-in-hand with organized medicine to achieve that evidently not impossible goal of matching military medicine to its civilian counterpart. Both groups at the meeting, each having its own responsibility—the military to the country's defense and the A. M. A. to the health and welfare of the country as a whole—obviously tried to meet each other halfway. That the meeting brought forth worthwhile discussions on the majority of topics shows this liaison between the practicing physician (regardless of whether he is an A. M. A. member) and the Department of Defense to be an effective link for improving military medicine.

RURAL HEALTH

While illness in a patient may not be clinically different whether he lives in a rural or urban community, the factors concerning the prevention and treatment of his illness vary greatly when the patient is distant from the contributions of a city medical center. Conditions leading to good health in village and country living are admittedly different from those in the more urban parts of the United States. After consideration of the recent reports on air pollution along with crowded living conditions, which are epidemic potentials, it is not impossible to envy the rural citizen. On the other hand, the farmer or rancher usually must be his own public health department, while the city resident has many preventive health measures performed for him through such environmental controls as sewage disposal and through his safe and adequate water supply. Because the rural population has demonstrated its desire to utilize available preventive techniques and, even more so, to understand better how to make the best use of professionally qualified medical care when it is available, and in view of the fact there is insufficient distribution of competent health personnel and facilities in many of these isolated areas, the Council on Rural Health of the American Medical Association has been assisting receptive communities in solving their unique health problems.

The natural problems and influences of an isolated area are not limited to environmental sanitation and animal diseases related to man but also include special adjustments to climate, nutrition, and safety. Whether it be a farm or mining community, to use just two examples, the desire for proper health education seems to be the element making these particular locations warrant special medical study. Until people become aware of a scientific total medical care program, they may be susceptible to any unreliable and unscientific advice that offers relief of aches and pains. They are equally subject to the propaganda of organizations that capitalize on remoteness and keep from them those advances in health and sanitation that would benefit their mode of living.

Rural health is not a misnomer. It is an all-inclusive term describing the path to a more healthful way of life to the citizen in the country. It is basically a lay-sponsored movement to help independent communities help themselves to healthier living by obtaining the active participation of all concerned. First, there are the programs emphasizing the preventive aspects of health, including sanitation of the environment, carried out in cooperation with public health workers. This is the groundwork that stresses the idea of personal protection from future illness and at the same time prepares the population for the acceptance of proper medical care when it is offered. Second, there is the actual providing of medical care by the recruitment of physicians, dentists, nurses, and other ancillary health personnel. These persons, despite their missionary spirit, must feel that they are really wanted and that use will be made of their skills. An example of the success of a rural health program appears in the report of Overholt and the Tennessee Medical Foundation.[1] In this instance, existing cultural patterns of misunderstanding were overcome by providing quality medical care and by having this betterment introduced by, shared with, and then earnestly desired by those who were to benefit from this progress.

While the physician should not claim a privileged position in the rural health movement, he should be available to serve in these ventures and to aid those seeking professional assistance. To solve most, if not all, of the health problems of any rural community in a manner satisfactory to the largest number of its people, the medical profession in addition to its cooperative effort must at the same time insist on self-help, voluntarily contributed.

MEDICINE DISCUSSES WAR

With tension rising and spreading in Eastern Europe and the Middle East, the sadly neglected concept "civil defense" cannot be pushed aside in the United States. Again, the nation's physicians are in the forefront of a continuing civil defense effort, keeping pace with new developments in nuclear, biological, and chemical warfare in order that they may better serve their community and nation in case of attack.

The degree to which civil defense also is a personal matter to physicians is shown repeatedly in each year's hurricanes, floods, fires, and tornadoes—natural disasters wherein the death toll is sharply reduced only when local medical societies act on their civil defense blueprints.

Latest developments to adjust those blueprints are revealed elsewhere in this issue (page 1237) from Washington, D. C., in "The Doctors Who Talk About War." It is a report of last month's meeting of federal representatives with the Civil Defense Committee of the A. M. A. Council on National Defense.

1. Overholt, B. M.: Role of Organized Medicine in Development of Rural Health Plans, Am. J. Pub. Health 46:904-907 (Aug.) 1956.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Like many of you, I recently received a four-page brochure urging the compulsory coverage of physicians under the Old-Age and Survivors Insurance provisions of the Social Security Act. This brochure, which gives the subject a quick and easy, "once over lightly" treatment based on questionable facts and figures, is from the committee on social security for doctors of the Physicians Forum.

The source of this material should immediately cast doubt on the accuracy and objectivity of its message. Most physicians will recall that the Physicians Forum was the only medical organization in the country that supported national compulsory health insurance and will not look kindly on any cause that it supports. Nevertheless, this is an issue on which there is room for honest differences of opinion based on facts rather than propaganda. The stepped-up activity of the Physicians Forum should stimulate all members of the profession to learn the facts about compulsory social security coverage for physicians. The issue undoubtedly will be coming up again in the immediate future.

One thing I think we should keep in mind, in order to maintain the proper perspective, is the difference between this problem and an issue like the disability benefits enacted by Congress earlier this year in H. R. 7225. The latter, and similar expansions that surely will be proposed in the future, bring the Social Security Administration closer to regulation of medical care and will have a dangerous effect on the future shape of medical practice.

On the other hand, the inclusion or exclusion of physicians under OASI, while it is vitally important to us as individuals, cannot in itself stimulate further government intrusion in the field of medical care. The issue is primarily one of personal philosophy, economics, and preferred alternatives.

On this issue, the House of Delegates of the American Medical Association has stated its opposition to compulsory coverage of physicians under OASI, although it has made it clear that there is no opposition to voluntary coverage. On the basis of all available evidence, this policy is in accord with the opinion of the majority of American physicians. For example, the House of Delegates, at the 1955 Boston Clinical Meeting, recommended that state societies poll their memberships on this question. The results, as reported at the 1956 Chicago Annual Meeting, showed that 34 state and two territorial societies opposed compulsory coverage. Only three polls could be interpreted as favoring compulsory coverage, and two of those were inconclusive.

More recently, *Medical Economics* magazine reported in its September, 1956, issue on a nationwide survey of more than 10,000 self-employed physicians. This poll eliminated the possibility of voluntary coverage and offered a choice between compulsory coverage and no coverage. The result: 59.8% favored no coverage and 40.2% favored compulsory coverage. In my opinion, the percentage in favor of no coverage will become even greater if every self-employed physician will study this issue and acquaint himself with the black-and-white realities of costs, benefits, and future probabilities.

The majority of self-employed physicians do not retire. About six out of seven doctors now in the 65-75 age group are still in private practice. It is unjust and unreasonable to force physicians to pay taxes into a system from which most of them will get little or no retirement benefits. It is well to remember also that under social security either you collect retirement benefits or your family collects survivors' benefits. It cannot be both. It has to be one or the other. But you as a self-employed physician are not likely ever to see the retirement checks. And the facts show that you can get much better, sounder, and cheaper protection for your family through private insurance companies than you can through social security taxes. This is especially true for younger physicians.

As one last suggestion, I urge you to read and reread the two articles on this subject by Drs. Webster and Coffey that appeared in the Sept. 15 and 22, 1956, issues of THE JOURNAL. There you will find an exhaustive collection of facts, figures, and examples that will help you make a decision based on knowledge rather than propaganda. Your decision and that of your professional colleagues—made known in your county and state medical societies—will determine the future policy of your House of Delegates in the American Medical Association.

DWIGHT H. MURRAY, M.D., Napa, Calif.

MEDICAL NEWS

CALIFORNIA

Hospital News.—Construction has started on a $500,000 addition to the department of diagnostic radiology at Cedars of Lebanon Hospital, Los Angeles. The expanded facilities will enable the hospital to increase its x-ray service. A conveyor system from the x-ray rooms to the darkrooms for development and to the doctors' rooms for viewing and consultation will expedite the service.

Fatal Case of Plague Reported.—According to the state department of public health, California's first known case of bubonic plague in man since 1947 resulted in the death June 25 of a 43-year-old retired Navy chief petty officer, nine days after his apparent exposure to infected fleas while he was on an outing in Lockwood Valley and Sespe Gorge areas of Ventura County. An investigation by local and state health departments disclosed a number of mummified squirrels and rabbits in the area where the man had walked from his car to do target shooting at a deserted farm. Tests by the state department of public health laboratory confirmed the case as plague resulting from a virulent strain of Pasteurella pestis.

CONNECTICUT

Phi Delta Epsilon Lecture.—The Alpha Rho chapter of the Phi Delta Epsilon fraternity at Yale University School of Medicine, New Haven, will hold its 11th annual lectureship in Yale Medical Center, Nov. 28. The guest speaker, Dr. Gustave J. Dammin, chief pathologist, Peter Bent Brigham Hospital, Boston, will discuss "Current Studies on the Survival of Skin Homografts."

Annual Clinical Congress.—The 31st Connecticut Clinical Congress of the Connecticut State Medical Society and the Yale University School of Medicine, New Haven, will convene at the Hotel Statler, Hartford, Dec. 5-6. Dr. Dwight H. Murray, Napa, Calif., President of the American Medical Association, will deliver the dinner address Thursday, 7 p. m. Registration admitting to all sessions will be $5. Medical students, interns, and residents will be the guests of the congress, if properly certified. In the ballroom Wednesday morning, "Coronary Artery Disease—Physiologic Concepts—Surgical Operation" will be presented by Dr. Claude S. Beck, Cleveland, and "Treatment of Carcinoma of the Cervix" by Dr. Howard C. Taylor Jr., New York. Simultaneously in the Boston room "Modern Treatment of Leukemias and Lymphomas" will be the topic of Dr. William Dameshek, Boston, and "Streptococcal Infections—Their Management and the Prevention of Complications" that of Dr. Benedict F. Massell, Boston. Luncheon in the ballroom will be preceded by a clinicopathological conference conducted by Dr. Joseph E. Flynn, Columbia, Mo., with Dr. Damashek as discussant, and will be followed by a panel on the management of myocardial infarction, with Drs. Charles K. Friedberg and Irving S. Wright, New York, as collaborators and Dr. Beck as discussant. At 3:15 p. m. the Hezekiah Beardsley Pediatric Society will present "Bilirubin: A Toxic Substance" by Dr. Richard L. Day, Brooklyn, in the ballroom; "The Therapeutic Team in Child Psychiatry" by Dr. I. Peter Glauber, New York, a program arranged by the Connecticut Society for Psychiatry and Neurology will be offered in the Boston-Buffalo rooms; and "Radio-Active Fall Out" will be discussed by Gordon M. Dunning, Washington, D. C., in the New York-Washington rooms. The Thursday morning program will include "An Evaluation of the New Oral Sulfonyl-Urea Drugs in Diabetes Mellitus" by Dr. Max Miller, Cleveland, and "Treatment of Nausea" by Dr. Stewart G. Wolf Jr., Oklahoma City (ballroom), and "Diagnosis of the Acute Abdomen in Children" by Dr. Orvar Swenson, Boston, and "Management of Urinary Tract Infections" by J. Hartwell Harrison, Boston (Boston room). Luncheon in the ballroom will be preceded by a clinicopathological conference conducted by Dr. Harry M. Zimmerman, New York, with Dr. Miller as discussant, and will be followed by a panel on "Gastric Ulcer: Medical Versus Surgical Management," on which Drs. Chester M. Jones and Francis D. Moore, Boston, will serve as participants and Dr. Wolf as discussant. The scientific sessions will end with "Medical Care Plan for Dependents of Military Personnel" (speaker to be announced).

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

DELAWARE

Research at State Hospital.—A research division that will function as an independent unit at the Delaware State Hospital, Farnhurst, was recently initiated. Dr. Fritz A. Freyhan, clinical director of the hospital, has been appointed director of research. The following projects have been approved: (1) a clinical-sociological study of schizophrenia in Delaware; (2) clinical investigations of the effectiveness of neuroleptic drugs; (3) the effectiveness of intensive psychotherapy in patients with chronic schizophrenic psychoses; and (4) cerebral blood flow and metabolism in psychiatric disorders (for which the National Institute of Mental Health has awarded a grant of $23,500 for a five-year period). The other projects will be financed from a special research fund appropriated by the state legislature.

FLORIDA

Geriatric Seminar at Sarasota.—The Sarasota and Manatee county medical societies and the Manasota Medical Foundation will present a Geriatric Seminar, Dec. 3-7, at the Orange Blossom Hotel, Sarasota. The seminar is approved for credit for postgraduate study by the American Board of General Practice. Drs. Hal M. Davison, Harold P. McDonald, Alva H. Letton, and T. Sterling Claiborne, Atlanta, Ga., will discuss a wide range of topics, including allergy in the aged, gallbladder disease, cardiac irregularities, coronary arteriosclerosis and thrombosis, cancer of the thyroid, teaching of psychosomatics, gastrointestinal and genitourinary disturbances, prostatic obstruction, and nutrition. There is no registration fee.

ILLINOIS

Pathologists Meet in Springfield.—The Illinois Society of Pathologists will hold its fall meeting Dec. 1 at St. Johns Hospital in Springfield, under the presidency of Dr. Dennis B. Dorsey, Danville. A slide seminar, 9 a. m., will have as moderator Dr. Grant C. Johnson, Springfield, and as panel members Drs. Harold D. Palmer, Springfield, and Paul E. Steiner and Mark C. Wheelock, Chicago. A luncheon and business meeting are scheduled for 1 p. m.

Clinics for Crippled Children.—The University of Illinois division of services for crippled children has scheduled the following clinics to which any private physician may refer children for consultative services:

Nov. 27, Effingham (rheumatic fever), St. Anthony's Emergency Hospital; Peoria, Children's Hospital.
Nov. 28, Aurora, Copley Memorial Hospital; Springfield (cerebral palsy), Memorial Hospital.
Nov. 29, Decatur, Decatur and Macon County Hospital.
Nov. 30, Chicago Heights (cardiac), St. James Hospital.

Chicago

Lecture on Cardiac Lesions.—The South Chicago branch of the Chicago Medical Society in cooperation with the Chicago Heart Association will present "Recognition of Common Cardiac Lesions" by Dr. Peter J. Talso, associate professor of medicine and assistant chairman, department of medicine, Stritch School of Medicine of Loyola University, Nov. 27 at 9 p. m. Audience participation and a social hour will follow the lecture, which will be delivered at the Illinois Central Hospital (cafeteria), 5800 Stony Island Ave. (phone: MIdway 3-9200).

Kaplan Lecture in Neuropsychiatry.—The Phi Delta Epsilon Foundation of Chicago announces that the 1956 Dr. Leo A. Kaplan Second Annual Lecture in Neuropsychiatry, "Influence of Psychosomatic Concepts on General Medicine," will be delivered by Dr. Theodore Lidz, professor of psychiatry, Yale University

School of Medicine, and psychiatrist-in-chief, Yale Psychiatric Institute, New Haven, Conn. Dr. Lidz, who is president-elect of the American Psychosomatic Society, will speak at the Drake Hotel, Nov. 29, 8 p. m. All physicians and interested persons are invited.

MASSACHUSETTS

Personal.—Dr. John M. Kinney, senior assistant resident surgeon, Peter Bent Brigham Hospital, Boston, has received the second annual Mead Johnson Award for Graduate Training in Surgery. The award, made through the scholarships committee of the American College of Surgeons, provides $3,000 annually for a three-year period. Dr. Kinney's studies are concerned with methods that could be utilized postoperatively either to increase the level of conversion of carbohydrates into energy or to provide increased amounts of carbohydrates for the metabolic process.

MICHIGAN

Dr. Karsner to Give Weller Lecture.—The Michigan Pathological Society has announced the establishment of the Carl V. Weller Lectureship in recognition of the contributions made by Dr. Weller in the fields of pathology and clinical pathology. The first lecture will be given in Ann Arbor, Dec. 8, by Dr. Howard T. Karsner, Washington, D. C., medical advisor to the Navy.

Personal.—Donald G. Marquis, Ph.D., chairman, department of psychology, University of Michigan, Ann Arbor, has been appointed a member of the National Advisory Mental Health Council, the surgeon general, U. S. Public Health Service, has announced. This council advises and makes recommendations to the surgeon general regarding activities of the National Institute of Mental Health.

MINNESOTA

Personal.—Dr. Edward A. Meyerding, St. Paul, executive secretary, Minnesota Tuberculosis and Health Association, has been awarded the William G. Anderson service award by the American Association for Health, Physical Education, and Recreation for his work in developing better health programs and environment for Minnesota school children. Dr. Meyerding's public health career began in 1909 with his appointment as director of hygiene of the St. Paul public schools.

NEW JERSEY

Society News.—The New Jersey Orthopedic Society recently elected Dr. Bernard M. Halbstein, Long Branch, president; Dr. Harold T. Hansen, South Orange, president-elect; Dr. Otto Lehmann, Long Branch, secretary, and Dr. John M. Naame, Atlantic City, treasurer.

NEW YORK

Meeting on Industrial Medicine.—The New York State Society of Industrial Medicine, will hold its annual meeting at the Hotel Roosevelt, New York City, Dec. 6, 4:30 p. m. "Radioactivity and Its Applications, with Particular Reference to Industry" will be discussed by Samuel A. Lough, Ph.D., deputy director, health and safety laboratory, Atomic Energy Commission; "Radioactive Fall-Out" by John H. Harley, Ph.D., chief, analytical branch, health and safety laboratory, AEC; and "Biologic Effects of Radiation" by Henry A. Blair, Ph.D., director, atomic energy project, University of Rochester School of Medicine and Dentistry. Cocktails and dinner are scheduled for 7 p. m. Requests for reservations should be sent to Dr. Harry E. Tebrock, New York State Society of Industrial Medicine, 1740 Broadway, 14th Floor, New York 19.

New York City

Conference on Mental Hygiene.—All directors of clinical laboratories and senior pathologists of the New York State Department of Mental Hygiene have been invited to participate in a one-day conference at the New York State Psychiatric Institute, Nov. 30, 9 a. m.-5 p. m. The program will feature a neuropathological seminar on diagnostic problems and unusual neuropathological conditions; a symposium on liver pathology in relation to recently used pharmacological therapy in mental disorders; and a series of scientific papers on clinical-pathological reports.

NORTH CAROLINA

Annual Gaston Symposium.—Dr. Nicholson J. Eastman, professor of obstetrics and director of the department of obstetrics at Johns Hopkins University School of Medicine and obstetrician-in-chief at Johns Hopkins Hospital, Baltimore, will be the guest speaker for the fifth annual Gaston Memorial Hospital Symposium in Gastonia, Nov. 28. Dr. Eastman will speak at 4 p. m. on "Apnea Neonatorum." His topic for the evening meeting will be "Maternity Care in Global Perspective." All sessions will be held at the Masonic Temple.

OHIO

Grant for Leukemia Study.—The John A. Hartford Foundation has made a grant of $162,075 to the Toledo Hospital for a three-year study of the causes and treatment of leukemia. The study will be conducted under the direction of Dr. Bernhard Steinberg, director, Toledo Hospital Institute of Medical Research, in conjunction with a group consisting in part of a clinical hematologist, Dr. Muvaffak A. Atamer, and a biochemist, Leon Libenson, Ph.D. The investigation is a transference of the basic research done at the institute for the past 11 years.

Seminar on Obstetrics and Gynecology.—The Southwestern Ohio Society of General Physicians in collaboration with the Cincinnati Obstetrical and Gynecological Society and the University of Cincinnati College of Medicine, offers a seminar on obstetric and gynecologic problems Nov. 26, in the medical school auditorium (emergency call answering service, AVon 1-2568). Among the topics to be discussed are bleeding in early and late pregnancy and after delivery; management of prolapse of cord and of convulsions; amniotic fluid embolism; aspiration during anesthesia; abnormal vaginal bleeding before menopause and postmenopausal bleeding; and pelvic pain. A question-and-answer period is scheduled for 3:15 p. m.

OREGON

Society News.—Dr. Herman A. Dickel, Portland, president-elect of the Multnomah County Medical Society, was recently elected charter president of the Portland Psychiatrists in Private Practice, an organization designed to study the situations, information, and problems incidental to the private practice of psychiatry. Other charter officers are Drs. Siegfried R. Berthelsdorf, Portland, secretary-treasurer, and DeWitt C. Burkes, Portland, executive committee member.

Course on Allergy.—A postgraduate course on allergy will be given Dec. 3-5 in the auditorium of the University of Oregon Medical School, Portland, under the sponsorship of the division of allergy of the medical school, the Allergy Society of Oregon, and the American Foundation for Allergic Diseases. Guest lecturers will be Dr. Ethan A. Brown, assistant professor of pediatrics, Tufts College Medical School, Boston, president of the American College of Allergists, and editor of the *Annals of Allergy*, and Dr. Orval R. Withers, associate clinical professor of medicine. The program will include round-table discussions and clinical demonstrations. Enrollment is unlimited, with a tuition fee of $25 for the course. Eighteen hours of Category I credit will be allowed by the American Academy of General Practice.

PENNSYLVANIA

Philadelphia

Ex Residents' Dinner.—The annual dinner of the Philadelphia General Hospital Ex Residents' Association will be held at the Penn-Sherwood Hotel, Dec. 4, 7 p. m.

Dr. Parkinson Accepts Reappointment.—On the request of President Robert L. Johnson, LL.D., and the executive committee of Temple University, Dr. William N. Parkinson has agreed to forego retirement plans as dean of the medical school and vice-president of the medical center and to accept reappointment in this dual capacity for an additional three-year period. The request on the part of university officials was prompted in part by the current extensive 12 million dollar expansion program at the medical center. Dr. Parkinson, who came to the medical school as associate dean in 1926, has been dean since 1929.

TENNESSEE

Personal.—John P. Quigley, Ph.D., Memphis, has been appointed by the surgeon general to serve as a member of the selection committee for the senior research fellowships granted by the National Institutes of Health.

Convulsive Seizure Clinic.—The University of Tennessee College of Medicine, Memphis, has opened a Children's Convulsive Seizure Clinic in the Pediatric Clinic of the John Gaston Hospital under the direction of Dr. James G. Hughes, professor of pediatrics. The new clinic, limited to patients of the hospital's outpatient department, will provide comprehensive diagnosis and treatment for children with convulsive seizures and undertake intensive study of the affected children.

TEXAS

New Regulations on Radiation Exposure.—The Texas State Board of Health has adopted new regulations on radiation exposure, which became effective Sept. 1. The state health commissioner, Dr. Henry A. Holle, Austin, states that these regulations are consistent with the National Committee on Radiation Protection report, which was prepared on request from representatives of the American College of Radiology, the American Medical Association, and the U. S. Public Health Service. The following points summarize the principal aspects of these regulations: 1. It requires registration of all radioactive materials and radiation-producing machines, such as x-ray equipment, within 30 days of commencement of use. 2. It establishes certain definitions, terminology, and official radiation symbols. 3. It establishes standards for air, water, and other environment. 4. It requires designation of a responsible person to be in charge of radiological safety programs. 5. It requires personnel monitoring and maintenance of records and reports under certain specified conditions. 6. It requires labeling of hazardous material and identification of areas where radioactive material is stored. 7. It requires permission prior to dumping or burying of radioactive wastes. 8. It requires reporting of accidental release of radioactive material that leaves premises of the user. 9. It requires reporting of accidental exposures received by a person when dose exceeds five times the permissible amount. 10. It allows certain specified exemptions. These regulations do not apply to the kind or amount of radiation that may be applied to a person for diagnostic or therapeutic purposes by or under the direction of a physician or dentist.

WASHINGTON

State Medical Election.—Officers of the Washington State Medical Association include Dr. James H. Berge, Seattle, president; Dr. Milo T. Harris, Spokane, president-elect; Dr. Walter C. Moren, Bellingham, vice-president; Dr. Frederick A. Tucker, Seattle, secretary-treasurer; and Mr. Ralph W. Neill, Seattle, executive secretary.

WEST VIRGINIA

Society News.—Dr. Clark K. Sleeth, Morgantown, was recently installed as president of the West Virginia Heart Association; Dr. Lynwood D. Zinn, Clarksburg, was named vice-president; Dr. James H. Walker, Charleston, secretary; and Mr. R. E. Plott, Charleston, treasurer (reelected).

Panhandle Medical Jubilee.—The Eastern Panhandle Medical Society will celebrate its golden anniversary at a banquet at the Shenandoah Hotel in Martinsburg, Dec. 1. The speaker, Dr. Louis A. M. Krause, is professor of clinical medicine at the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, and a teacher of the history of medicine. A social hour will precede the banquet, and at the conclusion of the program there will be a reception and dancing.

Institute on Medical Practice.—An all-day postgraduate institute, regional meeting, sponsored by the West Virginia chapter of the American Academy of General Practice and the Eastern Panhandle Medical Society, will be held at the Shenandoah Hotel in Martinsburg, Dec. 2. The lecturers have been voted best in their respective categories, or as best all-around lecturers, by the seniors in the medical schools represented on the program:

Diagnosis and Treatment of Sciatica, Dr. Bernard J. Alpers, professor of neurology, Jefferson Medical College of Philadelphia.
Poisoning in Children, Dr. John E. Bradley, professor of pediatrics, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore.
Subject to be supplied, Dr. Robert J. O. Colley, professor of surgery, Georgetown University School of Medicine, Washington, D. C.
Subject to be supplied, Dr. Eleanor Delfs, associate professor of obstetrics, Johns Hopkins University School of Medicine, Baltimore.
Obesity, Dr. William Parson, professor of internal medicine, University of Virginia School of Medicine, Charlottesville, Va.
A Rational and Aggressive Plan for the Management of Acute Upper Gastrointestinal Hemorrhage, Dr. Charles M. Thompson, professor of medicine and head, department of gastroenterology, Hahnemann Medical College and Hospital of Philadelphia.
Modern Concepts of Toxemias of Pregnancy, Dr. Washington C. Winn, professor of clinical obstetrics and associate professor of clinical gynecology, Medical College of Virginia, Richmond, Va.

WISCONSIN

Personal.—Edmund Fitzgerald, Ph.B., LL.D., president, Northwestern Mutual Life Insurance Company, Milwaukee, has been appointed to serve on the National Advisory Health Council, the surgeon general, U. S. Public Health Service, announced Oct. 19. The council is composed of 12 nonfederal leaders in medical science and public affairs, with ex officio members from the Department of Defense and the Veterans' Administration. On the council's recommendation, the surgeon general awards grants to scientists in hospitals, universities, and other nonfederal institutions conducting research.

Symposium on Immunology.—The Milwaukee Academy of Medicine will present an all-day symposium on immunology at Marquette University, Brooks Memorial Union, Dec. 1. The faculty will include Drs. Frank J. Dixon Jr., University of Pittsburgh School of Medicine; Tzvee N. Harris, University of Pennsylvania School of Medicine, Philadelphia; William B. Sherman, Columbia University College of Physicians and Surgeons, New York; Carl V. Moore, Washington University School of Medicine, St. Louis; and Theodore L. Squier, Marquette University School of Medicine, Milwaukee. All physicians are welcome. There will be no registration fee. Luncheon will be served at the union. Reservations may be secured through the Milwaukee Academy of Medicine, 561 N. 15th St., Milwaukee 3.

WYOMING

State Medical Election.—Newly elected officers of the Wyoming State Medical Society include Drs. Joseph S. Hellewell, Evanston, president; Harlan B. Anderson, Casper, president-elect; Luther H. Wilmoth, Lander, vice-president; Benjamin Gitlitz, Thermopolis, secretary; and Carleton D. Anton, Sheridan, treasurer.

GENERAL

A. M. A. Seattle Clinical Meeting, Nov. 27-30.—Physicians who attend the Clinical Meeting in Seattle may decide which and how many of 21 panel discussions, 48 lectures and talks, 18 television clinics, 24 motion pictures, and 97 scientific exhibits they desire to attend. Much effort has been made to bring practical solutions to everyday problems with a panel discussion on office gynecology, lectures on office treatment of varicose veins and office treatment of mild depressions, and a motion picture on office management of arthritis.

The Scientific Program starts Tuesday morning and continues until Friday noon at the Civic Auditorium. On Tuesday evening, a special showing of a motion picture "The Medical Witness" will be presented at the Olympic Hotel, with introductory remarks by C. Joseph Stetler, Director, Law Department, American Medical Association; David F. Maxwell, President, American Bar Association; and David B. Allman, President-Elect, American Medical Association.

Capps Prize for Medical Research.—The Joseph A. Capps Prize for Medical Research ($300), founded by Dr. and Mrs. Edwin R. LeCount, is being offered by the Institute of Medicine of Chicago for the most meritorious investigation in medicine or in the specialties of medicine. The investigation may be also in the fundamental sciences, provided the work has a definite bearing on a medical problem. Competition for 1958 is open to graduates of Chicago medical schools who completed their internship or

one year of laboratory work within five years before Jan. 1, 1956, excluding their terms of service in the armed forces. Manuscripts must be submitted to the Secretary of the Institute of Medicine of Chicago, 86 E. Randolph St., Chicago 1, not later than Dec. 31. The manuscript of the prize paper, as submitted, will become the property of the Institute of Medicine of Chicago.

Committee on Disaster Studies.—The committee on Disaster studies, of the division of anthropology and psychology, National Academy of Sciences-National Research Council (2101 Constitution Ave., Washington, D. C.), was established as the result of a request made of the academy-research council by the surgeons general of the Army, the Navy, and the Air Force, that it "conduct a survey and study in the fields of scientific research and development applicable to problems which might result from disasters caused by enemy action." The committee maintains a clearinghouse on disaster research, publishes a roster of scientific personnel in the field of disaster research, and issues a newsletter. It makes grants to encourage research in disaster studies, advises with responsible officials on problems of human behavior in disaster, and reports on the results of disaster research. Both new reports and previously unpublished work are selected for publication. Members of the committee serve without compensation beyond their actual expenses. Activities are presently supported by a grant from the Ford Foundation and by a special grant from the National Institute of Mental Health of the Department of Health, Education, and Welfare. Grants for the work of the committee are received and administered by the National Academy of Sciences. Established by Act of Congress in 1863, the academy is a private nonprofit organization of scientists dedicated to the furtherance of science and to its use for the general welfare. Pursuant to a request made by President Wilson in 1916, the academy organized the National Research Council.

FOREIGN

Swedish-American Exchange Fellowship.—The American Cancer Society in cooperation with the Anti-Cancer Society of Sweden has completed plans for a Swedish-American Exchange Fellowship program that will encourage an interchange of American and Swedish cancer research scientists.

Hadassah Establishes Health Center.—Hadassah, the Women's Zionist Organization of America, has announced as an eighth anniversary gift to the state of Israel the establishment of a Community Health Station, equipped to provide preventive, diagnostic, and curative physical and mental health services, in the all-Arab village of Abu Ghosh on the Jerusalem-Tel Aviv Highway. The new program for Abu Ghosh will include the dissemination of the latest information about health and sanitation, the breaking down of cultural or environmental taboos interfering with sound physical or emotional health, vaccination and immunization, treatment of existing physical ailments including dental and eye care, and the treatment of emotional tensions within the family group.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 18-20. Sec., Dr. D. C. Gill, State Office Bldg., Montgomery 4.

ARKANSAS:* *Examination and Reciprocity.* Little Rock, Nov. 8-9. Sec., Dr. Joe Verser, Harrisburg.

CALIFORNIA: *Qual Examination for Reciprocity Applicants.* Los Angeles, Nov. 17. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

COLORADO:* *Examination.* Denver, Dec. 4-5. Final date for filing application was Nov. 2. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver 2.

CONNECTICUT:* *Examination.* Hartford, Nov. 13-15. Sec., Dr. Creighton Barker, 180 St. Ronan St., New Haven.

DELAWARE: *Examination.* Dover, Jan. 8-10. *Reciprocity.* Dover, Jan. 17. Sec., Dr. Joseph S. McDaniel, 225 So. State St., Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, Nov. 13-14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington 6.

FLORIDA:* *Examination.* Miami Beach, Nov. 25-27. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

IDAHO: *Examination and Reciprocity.* Boise, Jan. 7-9. Exec. Sec., Mr. Armand L. Bird, 304 Sonna Bldg., Boise.

IOWA:* *Examination.* Des Moines, Dec. 3-5. Ex. Sec., Mr. Ronald V. Sal, State Office Bldg., Des Moines.

KANSAS: *Examination and Endorsement.* Topeka, Dec. 12-13. Sec., Dr. Lyle F. Schmaus, 872 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 10-12. Sec., Dr. Russell Teague, 620 South Third St., Louisville 2.

LOUISIANA: *Examination and Reciprocity.* New Orleans, Dec. 6-8. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

MAINE: *Examination and Reciprocity.* Portland, Nov. 13-14. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, Dec. 11-14. Sec., Dr. Lewis P. Gundry, 1211 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, Jan. 15-18. Sec., Dr. Robert C. Cochrane, State Office Bldg., Boston.

MISSISSIPPI: *Reciprocity.* Jackson, December. *Examination.* Jackson, June. Asst. Sec., Dr. R. N. Whitfield, Old Capitol, Jackson.

NEBRASKA:* *Examination.* Omaha, June 17-19. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: *Examination and Reciprocity.* Concord, March 13-14. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW MEXICO:* *Examination and Reciprocity.* Santa Fe, Nov. 19-20. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Charlotte, Jan. 14. Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination and Reciprocity.* Grand Forks, Jan. 2-5. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination and Reciprocity.* Columbus, Dec. 18-20. Sec., Dr. H. M. Platter, 21 West Broad Street, Columbus 15.

OKLAHOMA:* *Reciprocity.* Oklahoma City, Dec. 7-8. *Examination.* Oklahoma City, June 11-12. Sec., Dr. E. F. Lester, 813 Braniff Building, Oklahoma City.

OREGON:* *Reciprocity and Examination.* Portland, January. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

PENNSYLVANIA: *Examination.* Philadelphia, Jan. 7-10. Act. Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, Jan. 3-4. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Examination and Reciprocity.* Columbia, Dec. 11-12. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* *Examination.* Sioux Falls, Jan. 21-22. Ex. Sec., Mr. John C. Foster, 500 First National Bank Bldg., Sioux Falls.

TEXAS:* *Examination and Reciprocity.* Fort Worth, Dec. 6-8. Applications for reciprocity must be complete and on file at least thirty days prior to the December meeting, and applications for examination must be complete and on file at least ten days prior to the meeting date. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

UTAH: *Reciprocity.* Salt Lake City, Nov. 20. *Examination.* Salt Lake City, July 11-13. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

VERMONT: *Examination and Reciprocity.* Burlington, Jan. 30, Feb. 1. Sec., Dr. F. J. Lawliss, Richford.

VIRGINIA: *Examination and Reciprocity.* Richmond, Dec. 5-7. Address: Secretary to the Board, 631 First St., S.W., Roanoke.

WASHINGTON:* *Examination and Reciprocity.* Seattle, Jan. 14-16 and Jan. 12. Sec., Mr. Edward C. Dohm, Olympia.

WEST VIRGINIA: *Examination.* Charleston, January. Sec., Dr. Newman H. Dyer, State Office Building No. 3, Charleston 5.

WISCONSIN:* *Reciprocity.* Jan. 9. *Examination.* Madison, Jan. 8-10. Sec., Dr. Thomas W. Torrey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

ALASKA:* On application in Anchorage, Fairbanks, Juneau and other towns. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

GUAM: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

HAWAII: *Examination.* Honolulu, Jan. 14-15. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

COLORADO: *Examination and Reciprocity.* Dec. 5-6, Lincoln and Denver. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

FLORIDA: *Examination.* Gainesville, Nov. 10. Sec., Dr. M. W. Emmel, University of Florida, Box 340, Gainesville.

OKLAHOMA: *Examination.* Oklahoma City, April 19-20. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, Dec. 1. Dr. Earl M. Palett, Sec., State Board of Higher Education, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, Dec. 7-8. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

WASHINGTON: *Examination.* Seattle, Jan. 9-10. Sec., Mr. Edward C. Dohm, Olympia.

WISCONSIN: *Examination.* Milwaukee, Dec. 1 and April 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

ALASKA: *Examination and Reciprocity.* Anchorage and Juneau, first week of February, April, June, August and November. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

AEC Awards Research Contracts.—The U. S. Atomic Energy Commission has announced the award of 20 unclassified life science research contracts in the fields of medicine and biology to universities and private institutions. In the medical sciences eight contract renewals for one year were awarded to allow for continuation of research already in progress. The following new contracts were awarded:

Cedars of Lebanon Hospital, Los Angeles: Chemical Studies on Connective Tissues of Animals Aged Prematurely by Irradiation (Assessment of Biochemical Age), Harry Sobel, Ph.D.

University of Colorado, Denver: A Study of the Combined Action of Certain Chemical Inhibitors of Metabolism with X-Radiation and Other Ionizing Radiations on the Growth of Certain Transplantable Malignant Tumors, Richard W. Whitehead and Raymond R. Lanier.

University of Illinois, Chicago: A Study on the Effects of Intragastric Irradiation with Beta Rays from Ruthenium^{106}—Rhodium^{106} in Patients with Malignant Disease, Armand Littman.

AIR FORCE

Air Force Residency Training.—Since July 1, 1956, a total of 180 U. S. Air Force physicians have entered residency training. Of this number, 154 are receiving their training in civilian hospitals and 26 are in training in military hospitals. At present, 23 physicians have been approved for residency training beginning in 1957, 14 in civilian hospitals and 9 in military hospitals. The Air Force has openings in almost all the clinical specialties for residency training beginning in July, 1957. In addition, a total of 155 Air Force physicians are taking sponsored internships, 96 in civilian hospitals and 59 in military hospitals.

NAVY

Rear Admiral Pugh Accepts University Position.—Rear Adm. Lamont Pugh, retired, surgeon general of the Navy from 1951 to 1955, has accepted a position as university physician at George Washington University, Washington, D. C. In his new position, he will deal mostly with the ailments that may beset the university students. Admiral Pugh was also commanding officer of the Naval Medical Center at Bethesda, Md., prior to his recent retirement from active service.

PUBLIC HEALTH SERVICE

Fluoridated Water Supplies.—The Public Health Service reported on Oct. 28 a marked increase in the number of people drinking fluoridated water to help protect children's teeth against decay. The latest tabulation shows that fluoridated drinking water is now furnished in this country to one-fourth of the people using public water supplies. During the first nine months of 1956, communities with a combined population of 6 million started fluoridating their water. In 1946 fluoridation was used in only 12 communities with a total population of 328,000. About 1,400 cities and towns with a total population of over 30 million people were using fluoridation at the end of September, 1956. Among the larger cities adopting this preventive dental health measure are Chicago; Philadelphia; Baltimore; Washington, D. C.; Pittsburgh; Cleveland; Milwaukee; San Francisco; St. Louis; and Buffalo.

Establish Center for Aging Research.—The Surgeon General, Dr. Leroy E. Burney, has announced the establishment of a Center for Aging Research in the National Institutes of Health, of which Dr. G. Halsey Hunt, at present associate chief of the Public Health Service bureau of medical services, has been appointed director.

The new center is a part of the Public Health Service's program to coordinate and accelerate all of its activities in the field of aging. The primary objective of the new program is to support additional research into the mechanisms involved in aging. A first activity will be to aid universities, medical schools, and other research organizations in establishing comprehensive research centers on aging, to be supported in part by research grants from the National Institutes of Health.

Creation of a Center for Aging Research in the Public Health Service is in line with the program developed by the federal government through the Federal Council on Aging and the member departments and agencies to coordinate all activities associated with the problem of aging.

Marion B. Folsom, Secretary of Health, Education, and Welfare, said, "There are more than 12 million people in this country today who are over the age of 65; by 1970, there will be more than 18 million. Many of our older citizens have special health problems. It is important that more be done to help solve these problems—to help older persons to greater independence and self-sufficiency and a life more free of disease and disability."

New Director of Clinical Center.—The surgeon general has announced the assignment of Dr. Jack Masur, Washington, D. C., as director of the Clinical Center at the National Institutes of Health in Bethesda, Md. Dr. Masur, who supervised the planning and building of the Clinical Center, assumed his new duties Nov. 1. The Clinical Center, which is said to be the largest facility of its kind in the world for research in the major diseases, was officially opened in July, 1953, and present facilities are about to be expanded to permit more research in neurological and cardiac surgery. Nearly 5,000 patients from all over the United States have been admitted to the center for study and treatment. It is the responsibility of the director of the Clinical Center to plan and use the facility so that patients will receive the best in medical care and, at the same time, the research programs will be carried forward with maximum effectiveness. Dr. Masur, a native of Augusta, Ga., entered the commissioned corps of the Public Health Service in 1943. Since 1951 he has been chief of the bureau of medical services in the surgeon general's office. He is president of the American Association of Hospital Consultants, a trustee of the American Hospital Association, and a member of the Joint Commission on Accreditation of Hospitals.

Four-Year Study of Cerebral Palsy and Mental Retardation.—Awards of more than $700,000 for a four-year study of the causes of cerebral palsy and mental retardation have been made to Yale University School of Medicine, New Haven, Conn., and to Brown University, Providence, R. I., the surgeon general of the Public Health Service has announced. These awards mark the beginning of a research program that, during the next 10 to 20 years, will attempt to identify factors responsible for cerebral palsy, mental retardation, blindness, and deafness.

Brown and Yale universities are the first of a dozen or more institutions that are expected to join this program. Yale's grant for the first year is $107,799; Brown's is $97,633. The surgeon general said plans contemplate that more than 1 million dollars yearly will be awarded to medical institutions under the program of the National Institute of Neurological Diseases and Blindness.

When the full roster of participating medical institutions has been achieved, it is expected that more than 6,000 persons will be studied annually. Mothers, infants, and children will be studied over a period of several years. The data to be collected by the participating medical institutions will include complete family history, pregnancy and prenatal histories, a detailed account of events at birth, and a complete physical and psychological history of each child during his initial stay at the hospital. Infants who show signs of stress, defects in development, or neurological problems will be selected for follow-up and will receive periodic psychological and neurological examinations. It is expected that these studies will clarify the role of heredity, brain injury and brain hemorrhage, lack of oxygen, difficulty in breathing, prenatal and postnatal infections, and anemia of the newborn in the development of neurological disorders.

The National Institute of Neurological Diseases and Blindness of the National Institutes of Health will analyze all data obtained by the cooperating medical centers and will submit the findings to each participating institution. The study at the Yale University School of Medicine will be under the general direction of Dr. Gilbert H. Glaser, and the project at Brown University will be directed by Dr. Eric Denhoff.

DEATHS

Elliott, B. Landis ● Kansas City, Mo.; born in St. Louis Dec. 18, 1890; Washington University School of Medicine, St. Louis, 1919; associate clinical professor of medicine (neurology) at the University of Kansas School of Medicine, Kansas City, Kansas; specialist certified by the American Board of Psychiatry and Neurology; past-president of the Jackson County Medical Society, and in 1942 received that organization's merit award for outstanding service to the Community Health League of Missouri; in 1936 vice-president of the Central Neuropsychiatric Association; in 1931 secretary, and in 1932 president, of the Missouri-Kansas Neuropsychiatric Society; vice-chairman, Section on Nervous and Mental Diseases, 1936-1937, American Medical Association; fellow of the American Psychiatric Association; member of the Kansas City Academy of Medicine, Kansas City Southwest Clinical Society, and the Missouri Society for Neurology and Psychiatry; served as chief of staff, St. Joseph Hospital, and head of the psychiatric department, St. Mary's Hospital; member of the staffs at St. Luke's, Trinity Lutheran, Menorah, Neurological, Research, and Kansas City General hospitals; in 1920 was with the Red Cross in Finland, and for this service was awarded the Order of the White Rose by the government of Finland; died in Lisbon, Portugal, Sept. 8, aged 65, of coronary thrombosis, while on a vacation in Europe.

Walsh, Jeremiah Henry ● Corning, N. Y.; born in Curtis, N. Y., Aug. 6, 1870; Niagara University Medical Department, Buffalo, 1894; an associate member of the American Medical Association, serving as a member of its House of Delegates from 1917 to 1924, a trustee from 1924 to 1933, and for many years secretary of the Board of Trustees; president of the Chicago Medical Society, 1924-1925; member of the Illinois State Medical Society; for many years practiced in Chicago, attending surgeon at the City of Chicago Municipal Tuberculosis Sanitarium, St. Anne's Hospital, and Norwegian-American Hospital, and consulting surgeon, St. Anthony de Padua Hospital; during World War I member of the exemption board, Selective Service; at one time a member of the board of education of Chicago; died Oct. 12, aged 86, of arteriosclerosis.

Muller, Henry Richard, Pittsfield, Mass.; Cornell University Medical College, New York City, 1913; at one time taught pathology at Johns Hopkins University in Baltimore; formerly associated with the Rockefeller Institute in New York City; served on the staffs of St. Luke's Hospital in Cleveland, Vassar Brothers Hospital in Poughkeepsie, N. Y., and the Doctors Hospital in New York City; on the staffs of the W. B. Plunkett Memorial Hospital in Adams and the Hillcrest Hospital, where he died Aug. 18, aged 69, of prolonged effects of injuries received in an automobile accident.

Alexander, Joseph H. ● Zavalla, Texas; Memphis (Tenn.) Hospital Medical College, 1891; an honorary staff member of Angelina County Hospital and Memorial Hospital, Lufkin; examining surgeon for the Southern Pacific Lines in Texas and Louisiana; died in Cleveland Aug. 25, aged 86, of coronary thrombosis.

Arkin, Archie Abraham ● Des Moines, Iowa; University of Manitoba Faculty of Medicine, Winnipeg, Manitoba, Canada, 1932; member of the American Academy of General Practice; on the staffs of Mercy and Iowa Lutheran hospitals; died in St. Mary's Hospital, Rochester, Minn., Aug. 14, aged 35, of pulmonary edema and myocardial infarction.

Baker, Cecil Heber ● St. Louis; St. Louis University School of Medicine, 1910; veteran of World War I; on the staff of the Lutheran Hospital; died Sept. 4, aged 69, of coronary thrombosis.

Barrett, Van F. ● Lakeview, Ohio; Western Reserve University Medical Department, Cleveland, 1895; died in the Mary Rutan Hospital, Bellefontaine, Aug. 31, aged 87, of coronary thrombosis.

● Indicates Member of the American Medical Association.

Bentley, Norman Philip ● St. Paul; Syracuse University College of Medicine, Syracuse, N. Y., 1909; member of the American Academy of General Practice; veteran of World War I; died Aug. 6, aged 68, of carcinoma of the lung.

Borow, Henry ● Bound Brook, N. J.; University of Arkansas School of Medicine, Little Rock, 1931; one of the founders and staff member of the Bound Brook Hospital, where he was a member of the board and where he died Sept. 9, aged 51, of lymphosarcoma.

Carter, Ross Stagg, San Diego, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1910; past-president of the San Diego County Medical Society; died Aug. 26, aged 73, of pulmonary emphysema and heart disease.

Collinson, Thomas Jefferson ● Tupper Lake, N. Y.; Queen's University Faculty of Medicine, Kingston, Ontario, Canada, 1908; died in the Royal Victoria Hospital, Montreal, Quebec, Canada, Aug. 14, aged 73, of myocardial infarction.

Curtis, Stephen Horace ● Troy, N. Y.; Albany (N. Y.) Medical College, 1915; in 1948 member of the House of Delegates of the American Medical Association, member of the American Society of Clinical Pathologists; fellow of the American College of Physicians; on the staffs of the Leonard and Samaritan hospitals; died Aug. 20, aged 62, of coronary occlusion.

Devol, Edmund, New York City; New York Homeopathic Medical College and Hospital, New York City, 1896; an associate member of the American Medical Association; died in the Roosevelt Hospital Aug. 28, aged 83.

Doran, William Thomas, New York City; Long Island College Hospital, Brooklyn, 1905; fellow of the American College of Surgeons; formerly on the faculty of University and Bellevue Hospital Medical College; an associate member of the American Medical Association; surgical director of Columbus Hospital; for many years on the staff of Bellevue Hospital; died in the Metropolitan Hospital Sept. 10, aged 78, of injuries received in an automobile accident.

Douglas, George R. ● Valparaiso, Ind.; the Hahnemann Medical College and Hospital, Chicago, 1901; for many years county health officer; served as health officer of Valparaiso; past-president of the Porter County Medical Society; on the staff of the Porter Memorial Hospital, where he died July 8, aged 82, of coronary occlusion.

Duggan, LeRoy Bates ● Houston, Texas; University of Texas School of Medicine, Galveston, 1928; clinical associate professor of medicine, Baylor University College of Medicine; specialist certified by the American Board of Internal Medicine; member of the American College of Gastroenterology and the American Psychosomatic Society; fellow of the American College of Physicians; veteran of World War II; on the staff of Hermann Hospital, where he died Aug. 27, aged 55.

Foster, Daniel Parsons, Detroit; Harvard Medical School, Boston, 1922; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; an associate member of the American Medical Association; for many years head of the division of metabolic diseases at Henry Ford Hospital, where he died Aug. 21, aged 64, of bronchopneumonia.

Foust, Earl Harland ● Eustis, Fla.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; member of the Michigan State Medical Society; died Aug. 27, aged 78, of pneumonia.

Ginsburg, Abraham ● New York City; Long Island College Hospital, Brooklyn, 1910; veteran of World War II; died Aug. 23, aged 68.

Glass, Bernard Robert, Napa, Calif.; Creighton University School of Medicine, Omaha, 1937; interned at the U. S. Marine Hospital, San Francisco; senior physician and surgeon on the staff of the Napa State Hospital in Imola; died in the Parks Victory Memorial Hospital Sept. 3, aged 45, of hemorrhage due to peptic ulcer.

Colley, Kyle Wood ● Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1921; on the staffs of St. Joseph's Hospital and the Mercy Hospital, where he died Sept. 6, aged 59, of cerebral hemorrhage.

Gordon, Adolphus Noble, Chicago; Meharry Medical College, Nashville, Tenn., 1894; on the staff of the Provident Hospital; died in the Albert Merritt Billings Hospital Sept. 22, aged 85, of post prostatectomy hemorrhage.

Guajardo, Javier G., Laredo Texas (licensed in Texas in 1926), died Aug. 21, aged 92, of bronchopneumonia and arteriosclerotic heart disease.

Hampton, John Erwin ● Newport, Tenn.; University of Tennessee Medical Department, Nashville, 1902; veteran of World War I and the Spanish-American War; died in the Valentine-Shults Hospital Sept. 2, aged 78, of nephritis and heart disease.

Hankins, Thornton Wilson ● Swoope, Va.; Medical College of Virginia, Richmond, 1906; died Aug. 31, aged 74, of cerebral embolism and arteriosclerosis.

Hauser, Robert Bain ● Royal Oak, Mich.; Rush Medical College, Chicago, 1908; past-president of the Oakland County Medical Society; an honorary staff member of the board of Highland Park (Mich.) General Hospital; served on the executive medical board of the William Beaumont Hospital, where he died Sept. 16, aged 72, of cerebral thrombosis.

Heaton, Thomas Henry ● Cambridge, Mass.; Tufts College Medical School, Boston, 1898; died Aug. 4, aged 81, of cerebral hemorrhage.

Henry, Albert Cleaver ● Wickford, R. I.; Hahnemann Medical College and Hospital of Philadelphia, 1930; past-president of the Washington County Medical Society; served as president of the staff of South County Hospital in Wakefield, and the Roger Williams General Hospital in Providence; school physician; died Aug. 15, aged 52, of coronary occlusion.

Hill, Reginald Lindsey, Lyndonville, Vt.; University of Vermont College of Medicine, Burlington, 1923; served as health officer; on the staff of the Brightlook Hospital in St. Johnsbury; died Aug. 9, aged 57, of heart disease.

Horrigan, Thomas Francis ● Detroit; Wayne University College of Medicine, Detroit, 1945; interned at the City of Detroit Receiving Hospital; formerly a resident at the Providence Hospital; served in the Medical Corps, Army of the United States; on the staff of the Metropolitan Hospital; died in Oscoda Aug. 13, aged 36, of coronary thrombosis.

Howard, Isaac B. ● Williamson, Ga.; Atlanta School of Medicine, Atlanta, 1909; for many years member of the county board of education; died Aug. 10, aged 81, of coronary thrombosis.

Howell, William Erastus ● Morristown, Tenn.; Tennessee Medical College, Knoxville, 1903; past-president of the Tennessee Medical Association; died Aug 28, aged 76.

Hubbard, Ralph George, Detroit; University of Michigan Medical School, Ann Arbor, 1926; an associate member of the American Medical Association; served on the faculty of his alma mater; on the staffs of the Woman's and Florence Crittenden hospitals, and the Mount Carmel Mercy Hospital, where he died Aug. 31, aged 57, of arteriosclerosis.

Jameson, Robert Emmet ● Phoenix, Ariz.; Milwaukee Medical College, Milwaukee, 1912; member of the Iowa State Medical Society; for many years practiced in Davenport, Iowa, and was secretary of the Scott County Medical Society; died Aug. 12, aged 76, of asthmatic bronchitis and emphysema.

Jenkins, Charles Rivington, Daytona Beach, Fla.; Long Island College Hospital, Brooklyn, N. Y., 1899; member of the Medical Society of the State of New York; died July 8, aged 77, of reticulum cell sarcoma.

Johnston, George P. ● Cheyenne, Wyo.; Medical College of Ohio, Cincinnati, 1891; member of the House of Delegates of the American Medical Association, 1903, 1917-1918, 1923, 1928-1929, 1931, 1933-1935, and 1937-1948; fellow of the International College of Surgeons and the American College of Surgeons; died Sept. 18, aged 93, of heart disease.

Jordan, Thomas Cook, Jr. ● Milledgeville, Ga.; Medical College of Georgia, Augusta, 1945; member of the Medical Association of Georgia and the American Academy of General Practice; formerly an officer in the Medical Corps, Army of the United States; died Aug. 13, aged 39, of coronary thrombosis.

Kaplan, Maurice Isadore ● Chicago; Washington University School of Medicine, St. Louis, 1910; assistant professor of radiology at the Chicago Medical School; member of the Radiological Society of North America; from 1914 to 1921 health officer, department of health; for many years on the staff of the Mount Sinai Hospital, where he died Sept. 6, aged 68, of pyelonephritis and diabetes mellitus.

Katzoff, Manuel, Norfolk, Va.; Baltimore Medical College, Baltimore, 1906; died in the Leigh Memorial Hospital Aug. 14, aged 71, of cancer of the stomach,

Keating, Francis Raymond, Philadelphia; Medico-Chirurgical College of Philadelphia, 1905; an associate member of the American Medical Association; for many years a medical referee for the Prudential Insurance Company; died in the Pennsylvania Hospital Sept. 9, aged 76, of heart disease.

Kellogg, Frederic Sherlock, Oxford, Miss.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the Medical Society of the State of Pennsylvania; an associate member of the American Medical Association; for many years practiced in Pittsburgh, where he was on the staff of the Western Pennsylvania Hospital; served as a member of the Lenawee County (Mich.) draft board; died in the Oxford Hospital July 31, aged 84, of heart disease.

Kidder, Frank Woodman Kinsman, Los Angeles; College of Physicians and Surgeons, Los Angeles, 1909; an associate member of the American Medical Association; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; died in the Hospital of the Good Samaritan Aug. 1, aged 69, of coronary heart disease and arteriosclerosis.

Kirov, Konstantin Vesselin ● Chicago; Leopold Franzens-Universität Medizinische Fakultät, Innsbruck, Austria, 1947; died in the Wesley Memorial Hospital July 27, aged 33, of Hodgkin's disease.

Knoch, Norbert Henry ● Glenwood Springs, Colo.; Denver and Gross College of Medicine, Denver, 1910; on the staffs of St. Joseph's and Childrens hospitals in Denver, and the Valley View Hospital; died July 27, aged 67, of heart disease.

Krieger, Henry Arthur, Madison, S. D.; Bennett Medical College, Chicago, 1909; died June 27, aged 74, of cerebral thrombosis and diabetes mellitus.

Langley, John Wesley, Granby, Mo.; College of Medicine and Surgery (Physio-Medical), Chicago, 1890; died Aug. 17, aged 89, of coronary disease.

Lavin, Francis Charles ● Carbondale, Pa.; Georgetown University School of Medicine, Washington, D. C., 1932; veteran of World War II; associated with St. Joseph's Hospital, where he died Aug. 10, aged 50, of a heart attack.

Leeson, Ernest Edward, Inverness, Fla.; College of Physicians and Surgeons of Chicago, 1894; died in the Veterans Administration Hospital, Bay Pines, July 6, aged 84, of arteriosclerotic heart disease.

Lewi, William Grant, Glendale, Calif.; Albany (N. Y.) Medical College, 1892; an associate member of the American Medical Association; member of the Medical Society of the State of New York; died Aug. 18, aged 86, of cerebral vascular accident.

Llewellyn, Charles Elroy ● Richmond, Va.; Medical College of Virginia, Richmond, 1916; member of the American Academy of General Practice; on the staff of the Johnston-Willis Hospital; died while on a vacation, Aug. 24, aged 63, of injuries received in an automobile accident near Parlin, Colo.

McClendon, John Irvin, Russell Springs, Ky.; University of Louisville Medical Department, Louisville, 1907; died Aug. 3, aged 76.

McCracken, Earl Joseph ● Whittier, Calif.; University of Louisville (Ky.) School of Medicine, 1947; interned at the Kentucky Baptist Hospital in Louisville, Ky.; served in the U. S. Air Force Reserve; on the staff of the Beverly Community Hospital in Montebello; died July 17, aged 42, of arteriosclerosis.

McGuire, Frank James ● Guilford, Conn.; Boston University School of Medicine, Boston, 1937; veteran of World War II; served on the staff of Hospital of St. Raphael in New Haven; died Sept. 1, aged 46, of sarcoma of the lung.

McKenna, Joseph Lawrence ● Grand Rapids, Mich.; University of Michigan Medical School, Ann Arbor, 1926; veteran of World War II; served on the staff of St. Mary's Hospital; died Aug. 25, aged 54, of pulmonary embolism.

Martin, John Reboe Bitner, Gap, Pa.; Miami Medical College, Cincinnati, 1903; died Aug. 21, aged 75, of acute coronary occlusion.

Meeker, Irving Avard, Upper Montclair, N. J.; New York Homeopathic Medical College and Hospital, New York City, 1898; an associate member of the American Medical Association; medical examiner, board of education, town of Montclair; died at Columbia-Presbyterian Medical Center, New York City, Sept. 15, aged 83, of cerebral thrombosis.

Melchiorre, Nicholas Vincent ● Philadelphia; Temple University School of Medicine, Philadelphia, 1930; on the staff of St. Agnes Hospital, where he died Aug. 28, aged 50, of acute myocardial infarction.

Meyers, Lloyd Rogers, Cumberland, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; member of the Medical and Chirurgical Faculty of Maryland; on the staffs of the Memorial and Sacred Heart hospitals; died Aug. 11, aged 65, of coronary thrombosis.

Miller, Lewis Israel ● Denver; Loyola University School of Medicine, Chicago, 1918; served as president of the Colorado Hospital Service; on the staffs of the Beth Israel, St. Anthony, and Childrens hospitals; died Aug. 13, aged 61, of acute coronary thrombosis.

Morgan, Burnice Earl ● Asheville, N. C.; University of Tennessee College of Medicine, Memphis, 1917; member of the American Academy of General Practice; for many years chairman of the Buncombe County Board of Education; past-president of the Buncombe County Medical Society and of the Tenth District Medical Society; veteran of World War I; on the staffs of the St. Joseph's, Aston Park, and the Memorial Mission hospitals; for a time a member of the board of trustees of Asheville-Biltimore College; died Aug. 14, aged 62.

Morgan, Loftus E., Baton Rouge, La.; Trinity Medical College, Toronto, Ontario, Canada, 1890; died at Our Lady of the Lake Hospital Aug. 21, aged 91, of coronary occlusion.

Neff, Robert Lee ● Joplin, Mo.; University Medical College of Kansas City, Mo., 1894; an associate member of the American Medical Association; fellow of the American College of Surgeons; on the staff of St. John's Hospital, where he died Aug. 23, aged 86, of coronary occlusion.

Orton, George Lee, Rahway, N. J.; Jefferson Medical College of Philadelphia, 1909; an associate member of the American Medical Association; past-president of the Union County Medical Society; formerly member of the board of health; on the staff of the Rahway Memorial Hospital of which he was a founder; died Aug. 11, aged 78, of coronary artery disease and heart block.

Payne, Richard Johnson ● St. Louis; St. Louis University School of Medicine, St. Louis, 1913; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Barnes, St. Louis Children's, and Missouri Baptist hospitals; died Aug. 28, aged 68, of coronary occlusion.

Rand, Paul King, Alexandria, La.; Tulane University School of Medicine, New Orleans, 1913; past-president of the Louisiana State Medical Society, of which he was a member; veteran of World War I; at one time on the faculty of the University of Wisconsin in Madison; past chief of staff, Baptist Hospital; on the staff of St. Frances Cabrini Hospital; died Aug. 7, aged 68, of heart disease.

Rayhill, John Wayland, Utica, N. Y.; Long Island College Hospital, Brooklyn, 1906; served on the staff of the Faxton Hospital, where he died Aug. 8, aged 79.

Robinson, William Herbert, Roaring Spring, Pa.; College of Physicians and Surgeons, Baltimore, 1907; died in Altoona June 28, aged 74, of arteriosclerotic heart disease.

Rogers, James Virgil ● Cairo, Ga.; Emory University School of Medicine, Emory University, 1921; member of the Grady County School Board; member of the American Academy of General Practice; died in Thomasville Aug. 25, aged 64.

Saunders, Robert Ritchie, Philadelphia; Jefferson Medical College of Philadelphia, 1892; an associate member of the American Medical Association; specialist certified by the American Board of Ophthalmology; died in the Jefferson Medical College Hospital Aug. 19, aged 84.

Schutzman, Benjamin Maxwell, Detroit; Detroit College of Medicine and Surgery, Detroit, 1930; died July 24, aged 50.

Seibert, David Allen, Los Angeles; Barnes Medical College, St. Louis, 1909; formerly associated with the U. S. Veterans Bureau; died in the Veterans Administration Hospital Aug. 7, aged 74, of pneumonia.

Sharkis, David, Philadelphia; Hahnemann Medical College and Hospital, Philadelphia, 1932; on the staff of the Hahnemann Medical College and Hospital; died in the Albert Einstein Medical Center, Northern Division, Aug. 20, aged 63, of hypertension.

Sharp, Jacob Sevier, La Follette, Tenn.; Tennessee Medical College, Knoxville, 1899; died Aug. 25, aged 84, of heart disease.

Simpson, Russell Edwin, Jr. ● Pasadena, Calif.; Stanford University School of Medicine, San Francisco, 1942; member of the American Psychiatric Association; veteran of World War II; on the staff of the Collis P. and Howard Huntington Memorial Hospital; died Aug. 6, aged 40.

Sims, Wayne Waldo Conway ● Seattle; University of Colorado School of Medicine, Denver, 1929; specialist certified by the American Board of Preventive Medicine; member of the American Academy of Dermatology and Syphilology; clinical assistant professor of public health and preventive medicine at the University of Washington School of Medicine; veteran of World War II; director of the venereal disease division of the Seattle-King County Department of Health; died Aug. 23, aged 52.

Smiley, Henry Chandler, Redondo Beach, Calif.; Denver and Gross College of Medicine, Denver, 1905; formerly practiced in Torrance, where he organized the Torrance District Health Center, which he served; died in Los Angeles July 15, aged 74, of heart disease.

Sneidman, George Irving ● Hartford, Conn.; Medical College of Virginia, Richmond, 1936; veteran of World War II; member of the American Academy of General Practice; on the staff of the Mount Sinai Hospital; died in the Hartford Hospital Aug. 23, aged 57.

Soper, Richard Watts, Hendersonville, N. C.; Sioux City College of Medicine, Sioux City, Iowa, 1898; formerly on the staff of the Veterans Administration Hospital in Augusta, Ga.; died in the Swannanoa unit of the Veterans Administration Hospital in Oteen Sept. 1, aged 87, of carcinoma of the prostate.

Thornton, Mary Bickings ● Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1904; emeritus professor of anatomy at her alma mater; member of the American Academy of General Practice; died in the Hospital of the Woman's Medical College of Pennsylvania Sept. 7, aged 75.

Thurston, Asa, Taylorsville, N. C.; University of Maryland School of Medicine, Baltimore, 1909; member of the Medical Society of the State of North Carolina; served in the state legislature; on the staff of the Alexander County Hospital; died in the Rowan Memorial Hospital, Salisbury, Aug. 24, aged 73, of arteriosclerosis.

Warinner, Junius Ernest ● Richmond, Va.; Johns Hopkins University School of Medicine, Baltimore, 1916; served overseas during World War I; member of the Richmond Academy of Medicine; for many years on the staff of the Grace Hospital; member of the board of directors of the Richmond Memorial Hospital; died Sept. 4, aged 64, of a heart attack.

Way, Lewis Richard, Traverse City, Mich.; Northwestern University Medical School, Chicago, 1922; veteran of World War II; died July 8, aged 58, of myocardial infarction and coronary arteriosclerosis.

FOREIGN LETTERS

BELGIUM

Poliomyelitis.—The Minister of Public Health and Family appointed a permanent commission of experts in poliomyelitis to consider the problems concerning this disease. As compared with the United States, with its annual morbidity rate in the last 10 years varying from 18 to 37 cases per 100,000 inhabitants, the morbidity rate during this same period in Belgium was from 3 to 11 cases per 100,000 inhabitants. A serologic survey was conducted to determine what age groups are most susceptible as a guide to a rational vaccination program.

Physicians and the Government.—The conflict between government and physicians reached a culmination, and the government's attempt to establish socialized medicine was thwarted. More than 80% of the physicians refused to obey the directions according to which the forms of the official social insurance should be used. Establishing a strictly medical organization in opposition to the governmental organization of sickness insurance, the Belgian Medical Federation on Oct. 1 established the National Service of Physicians. The physicians have refused to become mere clerks. The aim of the National Service of Physicians is to assure that all persons with modest income receive the necessary medical care, with their personal rights taken into consideration. The members of this association agree to respect the scale of fees established by the National Medical Service. The beneficiaries of the National Medical Service are all persons, whether insured or not, whose yearly gross income does not exceed 100,000 francs, with an increase of 25,000 francs for a wife and 10,000 francs for each additional dependent. By means of this purely medical association and without governmental interference, the medical needs of the population will be met.

Tuberculous Meningitis.—Durieu and co-workers reported to the Belgian Society of Scientific Studies that 87 patients with tuberculous meningitis, in 65 of whom the diagnosis was bacteriologically confirmed, were given intraspinal injections of streptomycin every day for three months and then injections every two days for three additional months. Intramuscular injections were then given for six months. The patients who did not respond to this treatment were given suboccipital or intraventricular injections. There were 42 survivors with a follow-up period of two to six years. Eight patients had relapses, and 4 of these recovered; 23 of the survivors were able to resume their work. Complete deafness was observed in 9 and severe disturbances of the labyrinth in 12 patients.

FRANCE

Hepatosiderosis in Alcoholics.—J. Lereboullet and co-workers, at the meeting of the Medical Society of the Hospitals of Paris on June 29, stated that hepatosiderosis is especially frequent in alcoholics (50%) and still more so in those with chronic hepatic cirrhosis (60%). Nevertheless, 35% of the patients with hepatosiderosis are not alcoholics and have livers that are histologically normal. The authors stress the fact that massive hepatosiderosis is found in an almost constant proportion of the population irrespective of the presence of cirrhosis or alcoholism but occurs more frequently in men. Such patients also have an excess of ferric pigments in the spleen, pancreas, myocardium, kidneys, and testes. It is not known whether this represents an early stage of diffuse hemochromatosis.

Idiopathic Auricular Fibrillation.—Maurice and co-workers, at a meeting of the Medical Society of the Hospitals of Paris on June 15, reported a series of 90 patients with idiopathic auricular fibrillation. The fibrillation was poorly tolerated in 85 of the patients in that, in addition to various functional disturbances, it gave rise to cardiac insufficiency in 34 patients, to left ventricular or global hypertrophy in 57, and to electrocardiographic anomalies in 38. The cardiac index was generally diminished, and in some patients this diminution was extreme. After digitalization, stabilization with quinidine under cover of anticoagulants was attempted in 68 patients and was successful in 47. In most of these there was no recurrence of the fibrillation. The return to sinus rhythm almost invariably led to spectacular improvement and almost always to a complete disappearance of the functional disturbances and the cardiac insufficiency and even of the radiological and electrocardiographic anomalies. On the other hand, the condition of the patients whose fibrillation continued generally deteriorated. It is therefore justifiable to make a cautious attempt to stabilize idiopathic auricular fibrillation with quinidine.

Brachyesophagus.—E. Roviralta, at the meeting of the Society of Pediatrics of Montpellier on April 23, showed that, for reasons principally anatomic and clinical, brachyesophagus in the nursling is almost always acquired. Its prevention should be based on a periodic examination of children presenting partial thoracic displacement of the stomach who are undergoing medical treatment. Gastric retention should be corrected by pylorotomy or section of adhesions. Phrenicectomy has been used successfully in the hemorrhagic form. Transhiatal fixation of the cardia should be reserved, as a prophylactic measure, for patients in whom gastric drainage or paralysis of the diaphragm has failed or for those in whom there are special indications.

Hypoproteinemia.—At the same meeting, J. Chaptal and co-workers said that hypoproteinemia in infants results in severe malnutrition, severe hepatic steatosis, and a decline in serum albumin and gamma globulin levels. Treatment is difficult, and the course is often unfavorable. The lack of certain amino acids interferes with the synthesis of many digestive, hepatic, and renal enzymes and gives rise to disturbances of pigmentation, xerophthalmia, parleche, and erythredema polyneuropathy. Chromatographic study of the blood and the urine demonstrates extreme plasma deficiency of amino acids and polyaminoaciduria linked apparently to an acquired enzyme disturbance of the renal tubule. In the course of hypoproteinemia due to hepatitis, a drop in the albumin level is associated with an increased gamma globulin level. The blood and urinary chromatograms show an abundance of amino acids poorly used by the altered liver in the plasma and a suprarenal polyaminoaciduria. In one patient with essential hypoproteinemia, the nitrogen balance was positive but inadequate. The balance was maintained only when 600 mg. of protein per kilogram of weight was given intravenously every day. The child died of shock after a transfusion. In both deficiency hypoproteinemia and essential hypoproteinemia, the protein deficiency was estimated at about 10 gm. of protein per kilogram of body weight.

Renal Diabetes.—M. Bernheim and co-workers (*Pédiatrie* 11:161, 1956) state that renal diabetes is a rare constitutional disease characterized by glycosuria without hyperglycemia, a normal glucose tolerance test, and absence of any disorders in urinary elimination of phosphorus and amino acids. True renal diabetes is characterized by a lowering of the T_{m_G} (maximum tubular excretory capacity for glucose) and abnormal glomerular filtration; pseudorenal diabetes occurs in subjects with a normal T_{m_G}. The possibility of a transformation of renal diabetes into diabetes mellitus, though improbable, requires further and prolonged observation of the cases.

Idiopathic Renal Acidosis.—Jeune and Charrat (*Pédiatrie* 11:295, 1956) state that idiopathic renal acidosis is of interest clinically because it corresponds to a certain number of cases of readily curable abiotrophy in infants, and theoretically because it poses the problem of the renal mechanisms in acidobasic regulation. No cause can be recognized with certainty, but one must think either of a particular sensitivity to vitamin D or of an immaturity of the renal tubules. The clinical aspect is most frequently that of a persistent anorexia and an arrest in growth occurring after the

The items in these letters are contributed by regular correspondents in the various foreign countries.

age of 6 months, with sudden episodes of acidosis. There is a discrepancy between blood acidosis and urinary alkalosis. The latter seems to be due to the incapacity of the proximal tubules to reabsorb bicarbonate ions, the functions of the distal tubules remaining intact.

Cystinuria.—C. A. Schiavini (*Pédiatrie* 11:181, 1956) states that modern methods of investigation of amino acid metabolism allow a differentiation between early cystinuria (or preferably lysinocystinuria) and cystinosis. Cystinosis, a rare disease, is recognized in infants by anorexia, arrest of growth, thirst, bouts of fever, and rickets, and in its late form by dwarfism, vitamin-resistant rickets, photophobia, and chronic renal disease. Hypophosphatemia and at times acidosis, increase of the alpha-2-globulins, and generalized hyperaminoaciduria may be present.

Viral Respiratory Disease.—R. Sohier and co-workers (*Pédiatrie* 11:831, 1956) studied the frequency of acute infectious bronchitis and pneumonitis caused by viruses, with use of serologic tests for their identification. These tests included the use of cold agglutinins, Streptococcus MG agglutinins, and complement-fixation tests for the ornithosis group of viruses, A and B influenza virus, the adenoviruses, and Q fever. In 26 of 173 patients under 6 years with bronchopneumonia and 23 of 61 such children from 6 to 15 years, the infection was due to a virus. In patients with other diseases positive reactions were found only in 1.1% of those under 6 and 3.3% of those from 6 to 15 years of age. The positive reactions in many cases ruled out the diagnosis that had been made on admission.

Cutaneous Lesions Following BCG Vaccination.—R. Bastin and co-workers (*Pédiatrie* 11:681, 1956) report that in two children, aged 3 and 3½ years, a generalized exanthema developed over five weeks after BCG vaccination. These eruptions in the first child showed some similarity with polymorphous erythema, and in the second they had a morbilliform appearance. The first child had a leukocyte count of 50,000 per cubic millimeter, with a predominance of lymphocytes, and the second had a leukocyte count of 14,000, with an eosinophilia. The authors believe the eruptions to be due to primary infection with the BCG.

IRELAND

Tuberculosis.—As a result of improved treatment, the death rate from tuberculosis fell from 91 in 1949 to 34 in 1954 per 100,000 population. The number of new cases reported fell from 7,552 in 1949 to 6,266 in 1954. The health department recommends that young persons who show a negative reaction to the tuberculin test should be offered BCG vaccination, particularly if they live in rural districts and wish to move into the towns or go abroad. Many Irish immigrants to Great Britain contract tuberculosis. In the last five years, 1,300 returned from Great Britain to be treated for tuberculosis.

SWITZERLAND

Chlorpromazine and the Biliary Passages.—In 3 to 5% of the patients treated with chlorpromazine, jaundice appears. This complication is, to a certain extent, independent of the dose of the drug, but when it appears it is almost always in the third or fourth week of treatment. Its severity and duration are variable. The clinical findings are those of biliary obstruction, despite the absence of any obstruction. Errors of diagnosis are frequent and often lead to operative exploration, which shows the principal biliary passage to be empty and free of obstruction. Needle biopsy of the liver shows the biliary canaliculi to be gorged with thick, dark bile, with the formation of a kind of biliary thrombi, while the hepatic cells appear to be intact. The spontaneous course of the jaundice is toward a cure, either rapid or after weeks or months. The pathogenesis of chlorpromazine jaundice has not yet been elucidated. F. Besson (*Schweiz. med. Wchnschr.* 86: 1020, 1956) concluded that chlorpromazine provokes in most patients a prolongation of the time of closing of the sphincter of Oddi, an irregular outflow of the bile in slow spurts, and a delay in the emptying of the gallbladder. It is therefore a matter of the creation of a genuine biliary dyskinesia of a special type, similar to cystic dystonia or atony, which appears even after cholecystectomy. There is apparently a hypertonia of the sphincter of Oddi in relation to the weakness of the biliary flow. The biliary emptying is therefore almost routinely disturbed by chlorpromazine, but without evident effect in most patients. Clinically, this effect of chlorpromazine helps to explain the digestive sluggishness and stubborn constipation that occur so often in the course of treatment, and it is associated with the reduction of peristalsis and of the secretory activity of the gastrointestinal tract.

Diuretic Effects of Certain Polysaccharides.—It appears from experiments made by Desaulles and Meier (*Schweiz. med. Wchnschr.* 86: 1060, 1956) that in intact rats subjected to overloading with water or saline solution, certain polysaccharides possess the property of inducing general diuresis and an elimination of sodium increasing in intensity with the sodium concentration of the overload. Potassium excretion is not modified. These effects are met with only in normal animals. They can be antagonized by aldosterone and disappear in animals deprived of their adrenals. It seems unlikely that the mechanism of action of these substances is due to a direct effect favoring the elimination of salt and water and that the effect disappears as a result of the increase of renal elimination of sodium and the passage of increased quantities of extracellular sodium into the interior of the cell as a result of adrenalectomy. As these special types of action, observed after the injection of polysaccharides, bacterial among others, cannot be reproduced with the help of any known hypo-physial or adrenal factor, it must be concluded that these effects are either the result of a complex inhibition of one or more of these factors or that they are due to some unknown factor.

Radioactive Isotopes.—J. H. Muller (*Med. et hyg.* 14: 351, 1956) showed that it is possible to inject strong preparations of radioactive zinc in the form of quasi-colloidal suspensions of an insoluble sulfur into the abdominal cavity of patients affected by severe peritoneal carcinosis of ovarian origin. In 1949, Muller used radioactive gold (Au^{198}), in a colloidal form, for intraperitoneal and intrapleural injections for the same purpose. Its half-life of 2.69 days is ideal for applications of this kind. In 1950, the author extended the indication for peritoneal administration of Au^{198} colloid (with artificial hydroperitoneum of about 400 cc. in patients without ascites) to all patients with ovarian cancer whatever their degree of operability, as a supplement to standard postoperative radiotherapy. This combined radiological treatment has already been applied to about 130 patients, with results that are proving more and more clearly favorable. In fact, in this group of patients, all those with operable lesions (stage 1) have remained free from relapses and only 20% of the patients in stage 2 have had relapses. Intravenous injection of Au^{198} colloid results in a quasi-specific accumulation of radioactive particles at the level of the reticuloendothelial elements of the liver and the spleen. In one patient, Muller obtained, by means of such injections, the dramatic disappearance of an enormous lymphosarcomatous hepatosplenomegaly, and in various other patients a partial regression radiosensitive cancerous hepatic metastases.

UNITED KINGDOM

The Minister's Annual Report.—In his report on the National Health Service in England and Wales for 1955, the Minister of Health noted that the total cost of the service was 1,386 million dollars, an increase of 61.6 million dollars over the previous year. Of this sum, over 1,086 million dollars was met by the exchequer out of sums voted by Parliament. Only 100.8 million dollars was provided by contributions from the National Insurance Fund. This is equivalent to 12 cents out of each weekly total contribution for men, and it represents only a small fraction of the full weekly contributions paid by, or in respect of, insured persons. There is still a popular belief among the so-called working classes that their weekly contributions to the National Insurance Fund defray the entire cost of the National Health Service, which many of them use so freely. The minister's report shows that the contributions from the National Insurance Fund covered only 7% of the total gross cost of the service. Other sources

of income were as follows: 19.6 million dollars paid by patients for dental treatment and dentures; 14 million dollars paid by patients for eyeglasses; and 13.8 million dollars paid by patients for drugs and appliances. This last sum is made up of the 14 cents that must be paid by each patient on every prescription dispensed for him under the service.

The hospital and specialist service costs 778.4 million dollars, which is just over 56% of the entire cost of the service. Hospital waiting lists, numbering only 453,000 persons, were the lowest recorded since the inauguration of the service. This decrease was most marked in the field of tuberculosis; the waiting list fell by 54% (from 3,017 to 1,387). In most areas, there are now no waiting lists for patients with tuberculosis. In spite of the fact that there was no increase in the number of hospital beds, the number of inpatients rose by 18,000, reaching a total of 3,600,000. The striking improvement in the tuberculosis situation is illustrated by comparing the 1955 figures with those of 1949. In the latter year, there were 19,908 deaths from tuberculosis, of which 17,559 were respiratory; 52,041 reported cases, of which 44,480 were respiratory; and a waiting list of 10,986. However, in 1955 there were only 6,492 deaths from tuberculosis, of which 5,837 were respiratory; 38,134 reported cases, of which 33,580 were respiratory; and a waiting list of 1,387. This vast improvement has made it possible to bring to an end the Swiss Sanatorium Scheme introduced in 1951 to relieve the strain on the sanatoriums in this country. Under that plan, 1,025 patients were sent to Switzerland for an average stay of six months at a total cost of just over 1.036 million dollars.

The number of full-time and part-time consultants rose by 2.1%, thus bringing the total to 6,650. These range from 801 in general medicine down to 44 in neurosurgery. The number of administrators fell by about the same percentage, but they still number over 28,000. The general medical service costs 147 million dollars. The number of principals in general practice under the service rose slightly, making a total of 18,832, of whom just under 7,000 practiced without an assistant or a partner. Of those in partnership, practically 10,000 were in partnerships of two or three, and only 289 were in partnerships of six or more. More than half of the assistants in general practice were 30 years of age or under, and nine were 76 years of age and over. Only 1,545 general practitioners attended refresher courses during the year. The pharmaceutical service cost 120.4 million dollars. During the year, 226,116,091 prescriptions were dispensed by pharmacists; this was 7,500,000 more than in the previous year. The average cost per prescription was 61 cents. The number of spectacles supplied was 4,500,000, and about 170,000 new and repaired hearing aids were supplied. The total number of persons now using hearing aids is 428,520.

Hospital Helicopter Landing Grounds.—Four hospitals in Cornwall are to have helicopter landing grounds in order to reduce the time taken in getting injured persons to the hospital by the R.A.F. Search and Rescue Service. This service, which was originally designed to rescue air crews that crashed in the sea, is now being used to an ever-increasing extent to rescue anyone in difficulty at sea or stranded on rocks. As Cornwall is one of the favorite playgrounds of England, with a coast line as noted for its dangers as for its beauty, every summer a number of persons lose or almost lose their lives in such accidents as falling down cliffs or getting stranded on rocks at high water. In the past, such persons, when rescued by helicopter, have first had to be taken to the helicopter base and then transferred to an ambulance to be taken to the hospital.

Vivisection.—The annual return of experiments on living animals, published by the Home Office, shows that 2,476,201 experiments were performed during 1955. The number of persons licensed to perform such experiments was 5,161, of whom 1,443 did not perform any during the year. About 87% of the experiments were performed without anesthetics. These consisted of inoculations, external applications, modifications of the animal's diet or environment, or the administration of a drug or toxin. In the study of cancer, 292 licensees performed 148,175 experiments. For public health purposes or for the diagnosis of disease, 180,306 experiments were made; these were usually simple inoculations. Over a million experiments were performed in the course of preparing and testing substances intended for use in the treatment of disease in man or animals.

Meals for Older Persons.—In September, 1955, a service of domiciliary meals for older persons was inaugurated in Rotherham. The first nine months of the service has been reported by Donaldson and Wales. (*M. Officer* 96:93, 1956). The plan is based on the assumption that every home has normally a certain amount of staple groceries and provisions and that if these were supplemented by the daily purchase of extra foodstuffs a full and varied diet could be provided for the patient. Of the 23 older persons selected for the program, all were over 80 years of age, lived alone, and had an income balance of less than $5.60 a week after the payment of rent and other weekly expenses. Twenty-one of the patients were housebound and 12 were bedfast. In each case the attendant at the home was given the sum of 88 cents a week with which to purchase supplementary food for five of the week's dinners. She was also given specimen menus as a general guide in achieving a balanced diet, but the patients were encouraged to suggest items for dinner so that their individual likes and dislikes could be respected. The general practitioners in charge of the patients were informed and consulted about the diet. At the end of the first nine months of the program, reports were obtained from the attending physicians; these showed a general improvement in the well-being of the patients. During the period, a total of 3,049 meals were served at a cost of $732. The two great advantages of the plan are that it provided for the personal predilections of the older persons and provided this by an existing service already operating in the home.

Postgraduate Courses for General Practitioners.—An account of a conference on postgraduate courses, organized by the College of General Practitioners, was published in *Research Newsletter* (no. 12) of the college. The Dean of University College Hospital London, reported that at his hospital they had been considering the appointment of general practitioners to various departments of the hospital and medical school. They were asking general practitioners to attend ward rounds and discuss with the students how, in their practice, patients might appear to them first. The dean agreed with the suggestion that a general practitioner should serve on the appointments committee, which selects students for the hospital. His hospital favored the suggestion that there should be a chair of general practice in each medical school.

Dr. J. G. McCrie, dean of the faculty of medicine at the University of Sheffield, reported that there were two representatives of the local faculty of the College of General Practitioners on the postgraduate committee of the university. This committee was responsible for arranging courses for general practitioners in and around Sheffield. In Sheffield it had been the custom for several years to provide for general practitioners, throughout the two winter terms, weekly ward rounds and clinical demonstrations. In response to 500 or 600 notices sent out, about 30 physicians usually attended. These were mostly the same persons each year. Evening lectures in pediatrics were popular. A general practitioner nominated by the local faculty of the college sat as a member of every selection committee. An arrangement was made by the professor of social medicine, in collaboration with the local division of the British Medical Association, for the attachment of final-year students to selected general practitioners for two weeks each. The program is voluntary, but few students fail to take advantage of it. The attachment was on a nonresidential basis, and Dr. McCrie considered that, if plans could be made that allowed for the student's residing in the physician's house, the program would be of much greater value. He wondered whether the setting up of a general practitioner unit attached to a university might not give a somewhat artificial view of general practice. No lectures were given in the university on general practice, but such questions as those about the structure of the National Health Service, statutory certificates, and medical ethics were included in the syllabus of certain classes. The local clergy have suggested that students should be instructed in cooperation with the clergy in the treatment of the sick.

Dr. Charles Newman, dean of the Postgraduate School of London, said that for general practitioners clinical evenings had proved successful originally but that the same people tended to come every time and that eventually attendance had fallen off. Lectures had not been satisfactory, as general practitioners did not find them clinical enough. Discussion panels were useful

as an occasional activity, but they were not flexible enough to form a regular weekly feature. Lecture-demonstrations had not proved successful nor had general ward rounds. In the end the best technique had proved to be to give special demonstrations in the wards: teaching over the bed and contrasting the condition of one patient, such as a patient with asthma with consequent bronchitis, with that of another patient, such as a patient with bronchitis showing bronchial spasm.

Dr. E. C. Warner, the dean of Charing Cross Hospital, described the plan in operation there. Students in the final six months of their clinical period are sent out to selected general practitioners for a course of instruction in general practice. A very important feature is that, in almost every case, the student lives with the physician during this time. It was found that the ideal period was three weeks. While the students are with the general practitioners, they examine as many patients as possible, both in the office and in the patients' homes. The patients rarely objected to the presence of the student. Although at first the students were averse to the program, they have become enthusiastic about it, and some have voluntarily arranged to stay with the physician for a fourth week. The cost of board and lodging is covered in part by the student and in part by the medical school.

WORLD HEALTH ORGANIZATION

Whooping Cough.—Although whooping cough is still often considered to be of relatively little importance, it kills more babies during the first year of life than all the other common diseases of childhood combined (Annual Epidemiological and Vital Statistics Report, vol. 9, no. 6, Geneva, World Health Organization, 1956). Deaths from whooping cough have shown a marked and continuous drop in the past 50 years, but the decrease has been much less than that observed in the death rates for other communicable diseases such as diphtheria, scarlet fever, and measles. Moreover, the drop in mortality began before the discovery of effective means of protection, and this fact has not been satisfactorily explained. Despite fewer deaths, the number of cases has not diminished and the disease affects as many people as ever. Whooping cough also appears to be unique among the infectious diseases, in that it usually strikes and kills more girls than boys. Recently there has been a rapid rise in reported cases of whooping cough from certain countries and territories, but this could be attributed to better medical reporting rather than to a real increase in the prevalence of the disease. The statistics collected indicate that whooping cough affects a greater proportion of young children in southern (Egypt, Portugal, Italy) than in northern countries.

Accident Prevention.—The World Health Organization regional committee for Europe reports that, in Great Britain, 45 people on an average lose their lives every day as the result of accidents, 16 in some form of travel (14 on the road, 1 on the railways, and 1 in air or water transport), 5 at some place of work (2 in factories, 1 in coal mines, and 2 in farms, quarries, and other places of work), and 24 in and around the home (17 inside the home and 7 in ordinary pursuits around the home). In the Netherlands also, traffic accidents are not the most frequent cause of accidental death. In Italy, the pattern is similar. The average daily accident toll is 44 killed (7 at work, 20 in travel, and 17 at home and elsewhere). In Finland in 1955, 36% of all deaths in the age group 1 to 14 years were due to accidents. About half of these were drownings (unlike the pattern in Great Britain, where drownings are rare). In Germany, accidents in the home account for more than 30% of all fatal accidents. In Yugoslavia, among hospital patients, almost 20% of the deaths result from accidents. Rapid industrialization in that country has led to a serious increase in accidents.

In Norway, efforts are being made to reduce the number of drownings in open disused wells, and legislation that will make owners responsible has been drafted. In France during the last 15 years or so, burns and scalds have become less frequent but falls out of windows and from high structures have become more frequent. A new and growing hazard in the home is poisoning. On the one hand, there are insecticides and corrosive liquids that are kept in many homes, particularly on farms; on the other, there are dangerous medicines that the manufacturers have tried all too successfully to make attractive with bright wrappings, pretty colors, and sugar coating on the pills. In Iceland, drowning has been decreasing as a cause of death. Swimming lessons are compulsory, and by use of the Icelandic hot springs many bathing pools have been made in which even the smaller children are happy to test their courage and skill. Traffic accidents are being reduced in Austria by getting children to take part in controlling the traffic. In that country, children are also being brought into factories and other places where danger is present. An account was given of a large block of flats where the automatic elevator was used by children but did not cause any accidents. A committee of children was responsible for keeping it clean and in good running order.

The following points were stressed: 1. Information about fatal accidents is much more complete and accurate than the records of injuries that do not result in death. Accidental deaths are relatively frequent in children under 5 years of age and in persons over 60. 2. Fatal accidents have become relatively more frequent in recent years because of the decrease in deaths from infectious diseases. There is also an absolute increase due to hazards associated with increasing mechanization. 3. The available statistics deal almost exclusively with fatal accidents, but the nonfatal accidents, which are perhaps 100 times as common, give rise to a great amount of suffering, disability, and economic loss. 4. There is an urgent need for more intensive studies of nonfatal accidents, as the evidence suggests that their pattern differs from that of fatal accidents. For example, fatal injuries in the home tend to cluster around persons in the extremes of life, but the nonfatal accidents affect principally the housewife and the adolescent children. 5. Special attention should be given to preventive measures. Houses and household equipment should be designed for safety, especially electrical appliances and sources of heat. Children and elderly people should be protected from dangerous drugs, corrosive liquids, and other hazards. The committee laid great stress on education as the greatest single measure in the prevention of accidents. This includes the careful training of children at home and in school and especially giving them a sense of responsibility for their own safety. It comprises also the training of teachers and parents through films, radio, television, posters, and booklets.

Dr. Sutter Resigns.—Dr. Victor A. Sutter, assistant director-general in charge of advisory services in the World Health Organization, in Geneva, has resigned his position in order to accept an appointment as Minister of Public Health and Social Assistance in his own country, El Salvador. Dr. Sutter, a member of the WHO staff since 1950, studied at the National University of San Salvador and at Johns Hopkins University in Baltimore.

Regional Director for Europe.—The regional committee for Europe elected Dr. P. J. J. van de Calseyde as its nominee for the post of World Health Organization regional director for Europe. The post became vacant as the result of Dr. Begg's death earlier this year. Dr. Van de Calseyde's name will be sent for endorsement to the WHO executive board in January. At present he is director-general of health at the Ministry of Health, Brussels, Belgium.

Resistance of Insects to Insecticides.—Leadership in the stimulation and coordination of research throughout the world on the problem of resistance of insects to insecticides should be assumed by the World Health Organization, according to a group of experts. Great alarm has been caused by the appearance of resistance to such insecticides as chlorophenothane (DDT) among certain species of insects. In the housefly, resistance to insecticides is becoming universal. It is also of frequent occurrence in the body louse and exists locally in several species of mosquitoes. WHO should coordinate the different lines of research on the problem of resistance already being undertaken in laboratories scattered throughout the world; stimulate further research, particularly concerning the physiology, biochemistry, and genetics of the insects concerned; assure the publication and exchange of information and research results; and facilitate the procurement of qualified personnel and funds for research. Standard techniques should be adopted or developed for detecting and measuring resistance, and WHO should circulate information concerning new insecticides as it becomes available.

CORRESPONDENCE

PREMATURE VENTRICULAR CONTRACTIONS DUE TO RAUWOLFIA THERAPY

To the Editor:—The occurrence of premature ventricular contractions due to Rauwolfia serpentina therapy has been recorded. Wilson and Wimberly (*J. A. M. A.* 150:1363 [Dec. 3] 1953) reported four cases in which this phenomenon was observed. One of the patients under observation by the above authors was on digitalis therapy. This fact elicited discussion among us and prompted this investigation. Wilson and Wimberly regarded the etiology or the mechanism of production of the premature beats as problematical, but speculated that "the bradycardia may allow a so-called irritable focus in the ventricle to become manifest." One of us (C. J. S.) had the opinion that, if this were true, the phenomenon would be more manifest in patients on digitalis therapy, because of the altered myocardial irritability in such patients. Digitalis, although it exerts a depressant action on myocardial irritability, may increase the irritability of a focus and thus initiate or perpetuate an arrhythmia (Gross and Jezer: Philadelphia, W. B. Saunders Company, 1956, chap. 4, p. 80). It was thus concluded that, if the bradycardic action of Rauwolfia alkaloids permitted irritable myocardial foci to discharge, this action might be more frequent in digitalized patients. If this were true, then the produced bradycardia with premature ventricular contractions might be secondary to Rauwolfia therapy and, in digitalized patients, be confused with the common sign of digitalis intoxication.

This study comprises the observations made on 30 patients receiving Rauwolfia alkaloids. The powdered whole root was not used in this study. Fifteen of the 30 patients were selected because they had been on long-term digitalis therapy. The maintenance dose of digitalis was stabilized, and all patients were in good nutritional status, thereby eliminating, with clinical practicality, the factors of overdigitalization and/or electrolyte imbalance. All patients were maintained on their usual routine of digitalis therapy and diet and activity restriction, and were given either alseroxylon (Rauwiloid), reserpine, or Eskaserp in the commonly used dosages (alseroxylon, 4 mg. at bedtime; reserpine, 0.25 mg., four times daily; Eskaserp, 0.5 mg. daily). None of the patients under observation were informed of their participation in the study, and none were questioned regarding heart consciousness, unless they volunteered this information. No patient was regarded as having premature ventricular contractions, unless these were able to be heard on clinical examination or recorded electrocardiographically.

The 30 patients were divided equally into two groups, namely, those receiving and those not receiving digitalis. Of the 15 patients not receiving digitalis, 3 displayed premature ventricular contractions that disappeared on withdrawing the Rauwolfia medication. Of the 15 patients receiving both digitalis and Rauwolfia, 7 showed premature ventricular contractions. In five of these seven patients, Rauwolfia therapy was discontinued. In all five, the premature contractions disappeared. In one patient, digitalis therapy was discontinued and Rauwolfia continued. This patient continued to show premature ventricular contractions, which were frequent enough to give the clinical and electrocardiographic picture of pulsus bigeminus. Upon the appearance of this arrhythmia, digitalis therapy was restarted and Rauwolfia discontinued. This resulted in the restoration of normal sinus rhythm. In the final patient, therapy with both drugs was discontinued, and, although the premature contractions stopped, the signs of cardiac insufficiency gradually appeared. Restoration of digitalis therapy returned the patient to his usual state of health. It is interesting that this patient, who had mild benign systemic arteriolar hypertension, was later placed on therapy with a different form of Rauwolfia and tolerated it, without displaying premature contractions.

This study, though limited in scope, indicates that Rauwolfia serpentina therapy may produce premature ventricular contractions. It suggests, likewise, that this phenomenon occurs more frequently in digitalized patients. The most common arrhythmia produced by digitalis intoxication is the frequent occurrence of premature ventricular contractions. The appearance of this arrhythmia, in a patient taking digitalis, is an ultimatum to temporarily discontinue therapy with the drug (Stewart: New York, Paul B. Hoeber, Inc., 1952, chap. 3, p. 84). The present study would modify this dictum in patients receiving Rauwolfia compounds in addition to digitalis. In such patients, the premature contractions produced by Rauwolfia may well simulate an effect of digitalis intoxication, resulting in discontinuation of treatment with this drug, thereby upsetting well-balanced maintenance therapy. The appearance of premature ventricular contractions in 7 of 15 digitalized patients receiving Rauwolfia, in contrast to 3 of 15 patients receiving Rauwolfia without digitalis, is worthy of note. This observation should alert clinicians to the fact that Rauwolfia therapy may produce premature ventricular contractions in all patients but, more readily, in digitalized patients. The fact that such effect may be confused with the toxic effects of digitalis should stimulate additional and more extensive observations of this phenomenon.

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SIGNAL DEVICE TO AID PATIENTS WITH BULBAR POLIOMYELITIS

To the Editor.—I have been using a simple signal device for more than 10 days to help a patient with bulbar poliomyelitis who had a tracheotomy and who is completely paralyzed. The device enables the patient to signal the nurse or doctor when he is in distress. When both arms and legs are paralyzed and the voice is impaired because of a tracheal catheter, the patient needs help when he feels he is suffocating or has abdominal discomfort or when his heart is giving him trouble. To provide a means of signaling, I taped to the lower lip two small wire prongs of a hearing aid and connected them to a bell buzzer and to four 1½ volt dry cell batteries, so that the tongue could make contact with them and so ring the buzzer. An electronic resistor was introduced among the batteries so that no shock at the tongue was realized.

This patient's outlook improved immediately when he knew that he had a means of calling for help. In one instance, I was in the hospital corridor when his buzzer began to ring constantly. I put on a gown and mask and, on going in to see what the trouble was, found the nurse suctioning saliva and mucus out of his mouth. The nurse said that the patient's mouth had filled with saliva and had caused the buzzer to ring by closing the circuit. Now the lad has progressed to where he can talk, and he has told me how grateful he is to have something with which he can communicate with the nurse. This device may alert the doctor or nurse to some situation that might otherwise take the patient's life. Other patients with bulbar poliomyelitis have told me that the lack of communication with anyone early in the course of their disease was most distressing and that, if some means of communication could have been arranged, they would have been much less apprehensive. I hope that this simple device will be used to help dispel their fear from now on.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Naturopathy: Right of Naturopaths to Practice Obstetrics and to Be Examined by Committee of Naturopaths in Such Subject.—The petitioners sought to restrain the defendant licensing body from revoking, canceling, or calling in licenses previously issued to them as naturopathic physicians by filing an original petition before the Supreme Court of Utah.

The parties stipulated that the main group of petitioners have held licenses that allow them to practice as naturopathic physicians, together with the privilege, and what they claim is their right, to use drugs to perform minor surgery and to practice obstetrics. The principal problems are the right of the petitioners to practice obstetrics and the determination of the agency that is authorized to give the examination therein. The statutes of Utah provide for the issuance of licenses (1) to practice medicine and surgery in all branches thereof, (2a) to practice as an osteopathic physician without operative surgery, (2b) to practice as an osteopathic physician and surgeon, (3) to practice the treatment of human ailments without the use of drugs or medicine and without operative surgery in accordance with the tenets of the professional college of which the applicant is a graduate; if the applicant under (2b) or under this subsection successfully passes *the* examination in obstetrics, the license shall also set forth this right to practice obstetrics, (4) to practice obstetrics.

It will be observed, said the Supreme Court, that in addition to the right to practice as aforesaid, if the practitioner successfully passes *the* examination in obstetrics, the license shall then include this subject. From a reading of the statute, it is apparent that the use of drugs, medicine, and operative surgery is explicitly forbidden to these petitioners except as they may qualify for the use thereof by some method otherwise provided.

The petitioners contend that practitioners of naturopathy are qualified to use drugs, to perform minor surgery, and to practice obstetrics. To say this, said the court, is to leave in the hands of this profession the right to repeal the statute that governs their practice and thereby customize and shape the statute to fit them, rather than to require them to conform to the statute covering the "practice of medicine and surgery in all branches thereof." It is a doctrine of bending the law to the determination by a profession of what shall be the tenets and requirements of that profession, rather than a doctrine of the individual conforming to the prerequisites of the law. We are unable and unwilling to lend our approval thereto.

The defendants, of course, do not deny the right of the petitioners to practice obstetrics, if they pass the required examination. The petitioners assert that this examination should be given by their committee of naturopaths and as a part of the examination on the subject of naturopathy. The defendants contend that the subject of obstetrics should be examined upon as though it were being given to an applicant on the subject of obstetrics only. We believe, said the Supreme Court, that the legislature has answered this problem by the statutes pertinent to the matter.

It will be noted, the court pointed out, that the act says that those applicants for a license to practice naturopathy who successfully pass the statutory examination in obstetrics shall have as a part of their license the right to practice in that field. A subsequent section of the act, which sets forth the duties of the several committees established thereby, provides: "(9) For practitioners of medicine and surgery in all branches thereof, and for the practice of obstetrics only, a committee of five persons each of whom shall be a licensed practitioner of medicine and surgery in all branches thereof in this state and a graduate of a chartered medical college of recognized standing." Can there be any doubt what examination the legislature intended, asked the court, when it said *the* examination and then went on to provide how, and by whom, the examination shall be given? Are we to say that an applicant qualified in no other medical field shall be examined by the practitioners of medicine and surgery in all branches thereof, and these petitioners shall be subjected to a lesser or different form of examination? What harm can come to these petitioners if they are required to meet only the professional skill in this subject that would be required of a midwife? We see none. By saying that all applicants for a license to practice obstetrics shall take the same examination from the same class of committee, the law lends uniformity of requirements and thereby fairness to all. If this committee requires of midwives certain requisite skill, learning, and aptitude in the practice of obstetrics, for the protection of the public, is it not reasonable to believe the legislature intended that these petitioners should reach at least this standard of professional attainment? We believe the legislature so intended.

Accordingly, the Supreme Court held that naturopaths are entitled to practice obstetrics only if they have passed the examination given in that subject by the committee regularly set up to give such examination. The petitioner's request for injunction was therefore denied. *Alexander v. Bennett*, 298 *P(2d) 823 (Utah, 1956).*

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

The Council has authorized the publication of the following explanation of the classification of the residency training programs in general surgery, as adopted by the Conference Committee on Graduate Training in Surgery.

EDWARD L. TURNER, M.D., *Secretary.*

RESIDENCY TRAINING PROGRAMS IN GENERAL SURGERY

The Conference Committee on Graduate Training in Surgery approves residency training in general surgery under the following categories:

1. Programs of four or more years' duration in fulfillment of the residency requirement for certification by the American Board of Surgery in group 1 (*J. A. M. A.* 159:479-481 [Oct. 1] 1955; ibid. 162:411 [Sept. 22] 1956).

2. Programs of three years' duration in fulfillment of the residency requirement for certification by the American Board of Surgery in group 2 (*J. A. M. A.* 159:479-481 [Oct. 1] 1955; ibid. 162:411 [Sept. 22] 1956).

3. Programs of one year's duration integrated with an approved program of four or more years' duration, but not as the senior year.

4. Programs in specialized hospitals offering additional training following completion of an approved residency in general surgery. (The American Board of Surgery will accept training in these hospitals toward meeting the practice requirement for group 2 candidates.)

In the Internship and Residency Number of THE JOURNAL (162:378-382 [Sept. 22] 1956), lists of residencies in the first three categories, corrected to the date of submission of copy to the printers, were published. Since that time the conference committee has granted approval to certain hospitals in the fourth category. When this action has been approved by the three organizations whose representatives compose the committee—the American Board of Surgery, the American College of Surgeons, and the Council of Medical Education and Hospitals of the American Medical Association—a list of these hospitals will be published in THE JOURNAL in January, 1957, together with a revision of the list in the third category, as approved by the committee.

In addition to the residencies in the four categories listed above and approved by the Conference Committee on Graduate Training in Surgery, the Council on Medical Education and Hospitals, acting independently, approves programs of one or two years' duration in preparation for the surgical specialties only. (Residencies in this category are not accepted by the American Board of Surgery in fulfillment of the residency requirements for certification by that board.)

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Rapid Diagnosis of Human Influenza Infection from Nasal Smears by Means of Fluorescein-Labeled Antibody. Ch'ien Liu. Proc. Soc. Exper. Biol. & Med. 92:883-887 (Aug.-Sept.) 1956 [Utica, N.Y.].

In the study of influenzal infection in ferrets by means of fluorescein-labeled antibody, it was possible to make a rapid diagnosis of influenzal infection during the acute stage of illness by detecting specific viral antigen in the desquamated nasal epithelial cells and macrophages in the nasal smears. This paper reports the application of this method to influenzal infection in humans. The method was applied to 20 patients during an outbreak of influenza A-prime infections, to 44 during an outbreak of influenza B, and to 23 patients with various acute febrile or respiratory illnesses. With a rise of fourfold or greater in titer of hemagglutination-inhibition (HI) antibody during convalescence or else the recovery of virus from human nasal washings used as diagnostic criteria for influenzal infection, the use of fluorescent antibody had an accuracy of 71% in an influenza A-prime and 38% in an influenza B epidemic. One false-positive diagnosis was encountered among 23 noninfluenzal infections. The use of labeled antibody on smears of nasal washings is less sensitive than the HI test, but a positive diagnosis could be made on the day the specimens were collected, while the HI test requires a delay of 10 to 14 days for collection of convalescent serum.

Hypertensive Pulmonary Vascular Disease. D. Heath and W. Whitaker. Circulation 14:323-343 (Sept.) 1956 [New York].

The authors describe six cases of severe pulmonary hypertension in four women between the ages of 21 and 58, one 24-year-old man, and one 12-year-old girl. The condition was complicated by a ventricular septal defect, Eisenmenger's complex, patent ductus arteriosus, atrial septal defect, and mitral stenosis, respectively, in the five adult patients; the child had idiopathic pulmonary hypertension. The clinical picture was dominated by symptoms and signs characteristic of pulmonary hypertension, which often masked underlying cardiac anomalies. Symptoms of severe pulmonary hypertension were breathlessness on exertion, frequent cough and colds, chest pain of anginal type, blueness of the lips and nails, and abdominal distention and swelling of the ankles due to congestive cardiac failure. Hemoptysis, hoarseness, jaundice, syncopal attacks, and palpitation occurred less commonly. Signs associated with pulmonary hypertension were giant "a" waves in the jugular venous pulse, a parasternal heave, a systolic lift over the right ventricular outflow tract, a palpable second sound in the pulmonary area that was loud and closely split on auscultation, a Graham Steell murmur, and a pulmonary systolic click. In addition, central and peripheral cyanosis, clubbing of the fingers, jaundice, signs of congestive cardiac failure, and cardiac murmurs occurred. The electrocardiogram usually showed clockwise rotation of the heart and the ventricular pattern of right ventricular hypertrophy. On radiological examination there was evidence of right ventricular hypertrophy, increased prominence of the pulmonary artery and its main branches, and decreased peripheral pulmonary vascular markings. Angiocardiography revealed a dilated pulmonary artery and a coppicing effect in the small branches of the pulmonary vascular tree. The flow of dye through these dilated vessels was abnormally slow. It allowed abnormal flows to be visualized and previously unrecognized cardiac defects to be demonstrated. Cardiac catheterization showed pulmonary artery blood pressures approaching or exceeding systemic pressures and occasionally revealed intrinsic cardiac defects.

Five of the patients died and autopsy was performed in all of these. The definitive pathological changes in the pulmonary vasculature were a distinct muscular media with two elastic membranes in the pulmonary arteriole and medial hypertrophy in the muscular pulmonary artery. Frequently in these vessels there was abnormal proliferation of intimal fibrous tissue with partial or complete occlusion of the lumen, adventitial fibrosis, and medial necrosis. Occasionally there was aneurysmal dilatation of thin-walled branches of the muscular pulmonary arteries.

Patients with pulmonary artery blood pressures chronically elevated to levels approaching or exceeding systemic pressures demonstrate a distinct clinicopathological entity for which the term hypertensive pulmonary vascular disease is proposed.

Peroral Maintenance Treatment of Pernicious Anemia with Vitamin B_{12} and Intrinsic Factor. H. Olsen. Ugesk. læger 118:895-897 (Aug. 2) 1956 (In Danish) [Copenhagen, Denmark].

Twelve patients with pernicious anemia who were treated from the start with vitamin B_{12} and intrinsic factor by mouth and reacted well to the treatment were examined after from 10 to 34 months of treatment. The blood status was satisfactory in all cases, and the neurological symptoms present at the beginning of treatment had disappeared. No new neurological symptoms attributable to the hematological disease had developed.

Constrictive Pericarditis: A Review and Long-Term Follow-Up of 78 Cases. J. C. Dalton, R. J. Pearson Jr. and P. D. White. Ann. Int. Med. 45:445-458 (Sept.) 1956 [Lancaster, Pa.].

Dalton and associates reviewed the clinical aspects of 78 patients with constrictive pericarditis, of whom 59 were males and 19 females. Sixty-five of the patients were operated on, and 42 of these are still living. Six have been followed for over 20 years, 10 for over 10 years, and 11 for over 5 years. All of the patients followed over 20 years are living normal, unrestricted lives. There were several operative deaths among 61 patients who underwent 71 operations. Of the seven patients who were operated on more than once, two died. Excellent results were obtained by operation in 32 of 64 patients and fair results in 13 (14 operations); no improvement resulted in 5 of the patients. The two groups of patients who obtained excellent and fair results were compared with regard to their preoperative status. The only positive correlation was that 29 of the 32 patients in the "excellent result" group were in sinus rhythm preoperatively, while three had atrial fibrillation. Of the 13 patients classified as having "fair results," only five were in sinus rhythm preoperatively, while eight had either atrial flutter or fibrillation as their basic rhythm. It is interesting that all six patients who had been followed for over 20 years and who are considered as having excellent results had normal rhythm preoperatively and at last examination in 1955.

Duration of symptoms, heart size, and calcification of the pericardium were compared in the two groups and showed no significant differences. Dyspnea on exertion, ankle edema, and abdominal swelling, in that order, are the most frequent complaints at the onset and as the constrictive pericarditis progresses. Among the physical findings, hepatomegaly and distention of the neck veins remain the most common. A systolic blood pressure above 130 mm. Hg was found in only one patient preoperatively, whereas wide pulse pressures were not rare (greater than 50 mm. Hg in 9% of cases). Systolic blood pressures commonly rose postoperatively, but no patient became seriously hypertensive. Cardiac enlargement was present in one-half of the patients. Cardiac pulsations were diminished in four-fifths but were fluoroscopically normal in the other fifth of the patients. Abnormal electrocardiograms were present in every pa-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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tient; the T waves were abnormal in 100% and the P waves in 72% of those with normal rhythm. Atrial arrhythmias were common, having been found in 34 of the 78 patients; fibrillation was identified in 27, being constant in 19, while flutter occurred in 3, in 2 of whom it changed to fibrillation. Calcification was noted in the pericardium in 60% of the patients.

Serum Hepatitis Following Dental Procedures: A Presentation of 15 Cases, Including Three Fatalities. F. E. Foley and R. N. Gutheim. Ann. Int. Med. 45:369-380 (Sept.) 1956 [Lancaster, Pa.].

Various skin-penetrating procedures have been known to be followed by serum hepatitis. The members of the house staff of the Rochester General Hospital, Rochester, N.Y., first became aware of the appearance of hepatitis after dental procedures in 1952. The charts of all patients treated at that hospital for infectious or serum hepatitis between June, 1953, and June, 1955, were studied. Of 57 patients with viral hepatitis, 7 contracted serum hepatitis after blood or plasma transfusions. The remaining 50 patients ordinarily would have been considered as having infectious hepatitis. Fifteen of these patients, however, gave a history of a dental injection during the preceding one to six months and are referred to as the dental serum hepatitis group. These dental injections consisted of the injection of procaine during the process of extracting teeth in 13 patients and the filling of teeth in 2 patients. Two of the 15 patients had received penicillin injections at the same time as the procaine injections. The ages of the patients ranged from 18 to 71 years. The onset of illness in 14 patients was insidious in nature. The remaining patient had a rather acute onset. Malaise, fatigue, and anorexia, alone or in various combinations, were the first symptoms in all but three of the patients. Nausea and abdominal pains were next in frequency. Laboratory data obtained in the 15 patients were characteristic of viral hepatitis. Three fatalities occurred in this group. Heat sterilization of needles, syringes, and instruments is essential to prevent the spread of serum hepatitis. The danger of the use of multiple injection bottles is emphasized.

Lupus Erythematosus, Discoid and Systemic: One Disease. M. F. Allende. Postgrad. Med. 20:254-259 (Sept.) 1956 [Minneapolis, Minn.].

Allende presents clinical, histopathological, experimental, and therapeutic evidence to support the concept that chronic discoid lupus erythematosus and systemic lupus erythematosus are merely variants of a single disease. Chronic discoid lupus erythematosus should be considered as the mildest form of systemic lupus erythematosus. Patients with chronic discoid lupus erythematosus should be warned about the dangers of actinic radiation, of the use of potentially toxic drugs, of minor infections, and of the indiscriminate removal of so-called foci of infection. They should be checked at regular intervals with physical examinations supplemented by determination of the sedimentation rate of the erythrocytes, by complete blood counts, and by urinalysis. These measures should be supplemented by a search for the L. E. phenomenon if imminent dissemination is suspected.

Agammaglobulinemia. S. Aarseth. Tidsskr. norske lægefor. 76: 505-507 (Aug. 1) 1956 (In Norwegian) [Oslo, Norway].

A case of primary idiopathic agammaglobulinemia in a man aged 41 is the first in an adult observed in Norway. The patient manifested, from early childhood on, a tendency to infections of the respiratory tract. He had the usual childhood diseases, recurrent bilateral purulent otitis, and from the age of 16 on a purulent sinusitis. He has had pneumonia at least 14 times. There are bronchiectases with type 3 pneumococci. A purulent meningococcus meningitis in June, 1955, yielded to intensive penicillin and sulfonamide treatment. Pneumonia shortly thereafter was successfully treated with aureomycin. In December, 1955, he had meningitis due to type 3 pneumococcus; again treatment with massive doses of penicillin and sulfonamide was effective. At this time severe diabetes of the insulin-deficient type was discovered. Agammaglobulinemia was suspected because of the patient's unusual tendency to infections. Electrophoretic examination showed the patient to be practically without gamma globulin. In agammaglobulinemia the respiratory tract is primarily exposed to infection. Bronchiectases belong in the picture. No special tendency to tuberculosis is seen. Generalized vaccinia with a fatal outcome has been noted in agammaglobulinemia, and children with this anomaly should not be vaccinated against smallpox. Prophylactically, patients with the disease can be protected against infection by the administration of gamma globulin in doses of 100 mg. per kilogram of body weight monthly; an alternative is application of an antibiotic—slow-acting penicillin—or a sulfonamide. An accumulation of infections in a patient calls for paper electrophoretic examination of the serum. It is the simplest diagnostic method for clinical use. In the case in question the combination of agammaglobulinemia, severe diabetes, and extensive bronchiectases infected with pneumococci make the long-range prognosis doubtful.

SURGERY

Adrenalectomy for Intracranial Metastases From Carcinoma of the Breast. A. Clain and A. H. Hunt. Brit. M. J. 2:627-629 (Sept. 15) 1956 [London, England].

At the Royal Marsden Hospital over 90 adrenalectomies had been performed up to the end of 1955. In only two patients were cerebral metastases clinically evident. The first patient, a 37-year-old woman, had been subjected to radical mastectomy for anaplastic carcinoma of the left breast in August, 1948. Carcinoma of the whole of the right breast, with peau d'orange and a retracted nipple and extensive involvement of the axillary nodes was found in January, 1951. Bilateral oophorectomy was performed and a course of x-ray therapy given to the right breast and glandular areas. The local progress of the disease was arrested. Thereafter the condition remained unchanged until November, 1954. At that time personality changes were evident. Radiograms of the skull showed expansion and destruction of the pituitary fossa, presumably from erosion by growth. The left lung contained multiple metastases. A large quantity of ascitic fluid was present. She was given daily doses of 1,000 mg. of testosterone propylpropionate for three days and 50 mg. of cortisone for five days. Her diabetes insipidus was treated with pitressin. On Nov. 23, it was felt that she was fit for surgery. Both adrenal glands were removed at one operation. She made a slow but steady recovery. Her mental symptoms cleared up and the diabetes insipidus gradually improved, though she still required small doses of pitressin. She has remained reasonably well up to the time of this report, 22 months after operation.

The second patient, a 40-year-old woman, also had cerebral metastases after a right radical mastectomy for anaplastic carcinoma. Her neurological state likewise recovered rapidly after removal of the right adrenal, the left adrenal having been removed at the time of bilateral oophorectomy seven days earlier. The authors conclude that bilateral gonadectomy and adrenalectomy is at present the only treatment of value for patients with intracranial metastases from cancer of the breast. It should be attempted when possible, because these patients are otherwise doomed. Hypophysectomy, whatever its place may be in the treatment of the other manifestations of metastatic breast cancer, has no place in the palliation of cerebral metastases.

Observations of Human Adrenal Cortical Deficiency with Special Reference to Replacement Therapy with Cortisone. A. C. Hills, H. A. Zintel and D. W. Parsons. Am. J. Med. 21:358-379 (Sept.) 1956 [New York].

Adrenalectomies have been performed in the University of Pennsylvania Hospitals as an experimental therapeutic approach to severe hypertensive disease. The studies presented deal particularly with two aspects, namely, (1) whether surgically produced primary adrenal deficiency in man differs in kind or in degree from spontaneously occurring Addison's disease, and (2) to what extent cortisone (with or without supplementation with desoxycorticosterone) falls short of furnishing entirely satisfactory maintenance therapy for adrenal-deficient man. The results of a five-year study of 44 patients subjected to adrenalectomy are presented together with observations of 9 patients in whom Addison's disease occurred spontaneously. Cortisone, often supplemented by a small quantity of desoxycorticosterone, was given as replacement therapy. Steroid therapy is indispensable for the survival of persons who have been subjected to total adrenalectomy, but some patients with Addison's disease and some sub-

totally adrenalectomized persons can survive and maintain well-being without it. Such patients apparently enjoy a nearly normal basal rate of adrenal cortical secretion. The survival value of this secretion can be estimated as corresponding to the amount of steroid that will just maintain a totally adrenalectomized man in good general health (that is, assuming adequate salt intake, about 30 mg. of orally administered cortisone acetate daily, supplemented by 1 mg. of desoxycorticosterone acetate given by the buccal route.

Few patients with Addison's disease are totally destitute of endogenous adrenal cortical secretion. Approximately 5% of the total amount of adrenal cortical tissue normally present will produce enough secretion to sustain life under ordinary circumstances. This quantity of surviving tissue has, however, practically no capacity to increase its basal hormone output, and a patient without ample cortical reserve is imperiled by any stress unless exogenous hormone can then be supplied. Cortisone can maintain the life of totally adrenal-deficient persons indefinitely and can restore strength and well-being, but it does not provide a balanced replacement for the missing adrenal cortical secretion, of which cortisone and hydrocortisone are only partial constituents. There is no truly "physiological" quantity of cortisone, that is, there is no dose of cortisone that, on long-term administration to adrenal-deficient patients with or without a small supplement of desoxycorticosterone, will not be accompanied by certain signs of hypoadrenalism or certain manifestations of hypercortisonism or both. The signs of hypoadrenalism commonly encountered in such patients are melanosis, impairment of water diuresis, unresponsiveness to hypoglycemia, and sometimes salt waste, azotemia, and hyperkalemia. The signs of hypercortisonism are polyphagia, weight gain, and impairment of glucose tolerance. No fundamental distinction can be drawn between spontaneous and iatrogenic primary adrenal cortical deficiency. The incidence of melanosis has been strikingly lower in patients rendered adrenal-deficient by surgery than in persons with spontaneous Addison's disease, but this difference can probably be ascribed to the provision of cortisone to the former group from the time of origin of the adrenal-deficient state. However, although cortisone has antipigmentary properties in adrenal-deficient persons, the adrenal cortex must contain antipigmentary factors other than cortisone and hydrocortisone. Clinically detectable regeneration of adrenal cortical tissue occurred only once in a series of 27 patients subjected to subtotal adrenal resection.

On the So-Called Abscess Cancer of the Lungs. L. Morelli and L. Di Domizio. Arch. ital. chir. 81:181-204 (No. 3) 1956 (In Italian) [Bologna, Italy].

Cavitary cancer of the lung, or abscess cancer, is a type of bronchogenic carcinoma; it is characterized by a cavity of recent formation that contains purulent necrotic material. The authors observed 12 such cases of cancer, 8 primary and 4 secondary. Among the eight primary cases, histological examination demonstrated small-cell carcinoma in six patients and polymorphous carcinoma in one. Of the four secondary forms, three belonged to the polymorphous type and one to the small-cell type. Radiological examination was useful in the general diagnosis of cavitary suppuration, but it was not so useful in the diagnosis of carcinoma. Bronchoscopy was performed in all cases. Biopsy of metastatic supraclavicular lymph nodes confirmed the clinical diagnosis. Six patients underwent surgery: one explorative thoracotomy, three pneumectomy, one lobectomy, and one pneumotomy. Ten patients were over 45 years of age, one was 43, and another was 41; there were 11 men and one woman. The symptoms, which were almost the same in all cases, included cough with little expectoration always tinged with blood, fever, and dyspnea. In some patients symptoms had been present for 12 months and in one case for two years. Surgical intervention is necessary if the combined therapy for pulmonary suppuration gives no result in from four to eight weeks, especially if the patient is over 45 years of age.

The Aggressive Treatment of Metastases. E. Wilson. M. J. Australia. 2:292-297 (Aug. 25) 1956 [Sydney, Australia].

The author believes that, while the future treatment of metastases lies more with hormonal and other methods, surgical treatment holds the first place at present. Not only is surgery advisable after metastases have been detected clinically, but there is also a place for elective reexploration to search for and to deal with metastases before they are otherwise detectable. In the absence of metastases at the primary operation, elective reexploration of the abdomen should be considered within six months in patients with carcinoma of the colon, ovary, liver, pancreas, and rectum, and slightly earlier in those with carcinoma of the stomach. In all cases in which a second operation has already been required for the eradication of a metastatic mass and where there is no evidence of any other metastasis, an elective reexploration should be strongly recommended. Supraradical surgery has a place in the early stages of certain cancers rather than in the subterminal stages of the disease. However, supraradical surgery is occasionally indicated even for palliation. A case is described in which symptoms of hepatic insufficiency were temporarily relieved by litigation of the branch of the hepatic artery to that particular lobe destroyed by the metastases. The relief was probably due to the resulting increased blood supply of the lobe that contained most of the functioning hepatic tissue.

More study should be given to (1) the effects on cancer cells of substances that stimulate the growth or metabolism of normal cells, (2) the reasons why some malignant growths do not metastasize, (3) the use in "hormone-dependent" cancers of hormone therapy and of hormone exclusion operations, especially hypophysectomy produced by both surgical and medical means, (4) the place of elective reexploration in the management of intra-abdominal and other cancers, and (5) the positions of metastases in specimens removed from patients apparently cured by surgery. Such study would provide a basis for determining the extent of the operations to be employed for various cancers.

Scalene Node Biopsy: An Analysis of 42 Cases. W. W. Yang. California Med. 85:165-166 (Sept.) 1956 [San Francisco].

Scalene node biopsy was done in 42 patients with previously undiagnosed intrathoracic lesions. The basis of the scalene node or fat-pad biopsy is that lymph nodes anterior to the scalenus anticus muscle are connected with the mediastinal nodes. Thus intrathoracic disease involving the mediastinal nodes may often be reflected in the scalene nodes. The same is true of systemic disease directly involving the mediastinal nodes. The simple scalene node biopsy hence is a biopsy of the mediastinal nodes without the necessity of entering the thorax. A definite histological diagnosis was obtained in 25 of the 42 patients. Carcinoma of the lung was detected in nine patients, metastatic tumor to the lung in eight, pulmonary tuberculosis in three, lymphoma in three, anthracosis in one, and sarcoidosis in one. Scalene node biopsy is especially useful in patients with bronchogenic carcinoma. In this disease the value of this biopsy is twofold: 1. A diagnosis may often be obtained without thoracotomy. 2. In such cases, and also in those in which the diagnosis has been made by other means, the procedure is of value in determining the prognosis. When a scalene node biopsy is positive for cancer, there has been considerable extension of the carcinoma; operability is then questionable. Complications are rare in scalene node biopsy. Hemorrhage due to injury to the jugular vein occurred in one of the patients in this series, but it was readily controlled. Scalene node biopsy is a valuable diagnostic procedure.

NEUROLOGY & PSYCHIATRY

Subarachnoid Haemorrhage Due to Intracranial Aneurysms: Results of Treatment of 249 Varified Cases. W. McKissock and L. Walsh. Brit. M. J. 2:539-565 (Sept. 8) 1956 [London, England].

A survey of 461 patients with subarachnoid hemorrhage admitted to St. George's Hospital in London up to March 31, 1954, revealed that in 249 the hemorrhages were caused by an aneurysm. The data on the 249 patients with proved intracranial aneurysm associated with subarachnoid hemorrhage are analyzed in relation to the severity of the effects of the hemorrhage and the site of the aneurysms. The results of various types of surgical treatment are compared with those of medical treatment. The frequency of associated intracerebral, intraventricular, and subdural hemorrhage is given. The frequency and time of occurrence of repeated hemorrhage is considered, and the operation of carotid ligation is discussed. Very early investigation and treatment of

patients with a bleeding aneurysm seems advisable because a lower mortality has been shown to occur in cases handled in such a manner than is to be expected from the natural course of the disease. In medically treated patients with anterior communicating or middle cerebral aneurysms the natural death rate is over 90%. If even a few patients can be restored to reasonable health by surgical measures, the operative mortality rate should surely be assessed against the natural death rate of 90%, and so even a 50% operative mortality rate would be acceptable.

An Investigation of Neurosurgical Alleviation of Parkinsonism, Chorea, Athetosis and Dystonia. I. S. Cooper. Ann. Int. Med. 45: 381-392 (Sept.) 1956 [Lancaster, Pa.].

Cooper summarizes the current status of the neurosurgical treatment of several hyperkinetic disorders, particularly Parkinsonism. He reviews observations made in the course of 200 operations, 180 of which were performed for Parkinsonism. The remaining 20 were performed in patients with various other hyperkinetic disorders, which could be grouped as chorea, choreoathetosis, tension-athetosis, and dystonia musculorum deformans. Fifty-five of these operations consisted of surgical occlusion of the anterior choroidal artery; the other 145 were chemopallidectomies. The operation of anterior choroidal artery occlusion is best suited for young patients with postencephalitis Parkinsonism of long duration. It has the disadvantage of being dependent upon the vagaries of the anterior choroidal artery, but it may produce great benefit in a reasonable percentage of patients. Therefore, in selected instances, the risks of this procedure are justified.

Chemopallidectomy is of potential value in all types of Parkinsonism. Its technique has the advantage of being accurate, straightforward, and simple to execute. In fact, its simplicity could easily lead to abuse and incorrect usage. Chemopallidectomy provides an opportunity to select the correct subcortical site for destruction by the performance of an intracerebral procaine injection before the infliction of a permanently destructive lesion. Thus, the effect in a given patient can be predicted with a reasonable degree of accuracy. The risk of this operation is low, the mortality rate being less than 3%. The possibilities of lasting benefit are good—at least 70% at the present time. There is at present no cure for Parkinsonism. There is, however, the possibility of useful alleviation of many of its symptoms by neurosurgery. There is as much, if not more, justification for the neurosurgical treatment of Parkinsonism as there is for the neurosurgical treatment of intractable pain or of focal epilepsy. The approaches described are new, but their cautious and expert use will not only give relief to patients but will also increase the knowledge needed to advance the therapy of hyperkinetic diseases.

Prenatal Obstruction of the Fourth Ventricle. D. D. Matson. Am. J. Roentgenol. 76:499-506 (Sept.) 1956 [Springfield, Ill.].

Successful treatment of hydrocephalus depends upon an accurate knowledge of the location and type of obstruction to normal cerebrospinal fluid movement. Matson describes one type of hydrocephalus, namely, that due to prenatal obstruction of the foramens of Magendie and Luschka, in which the roentgenographic findings are pathognomonic. Obstruction of the normal foramens between the fourth ventricle and the surface subarachnoid pathways dating from early embryonic life falls into the category of congenital anomalies in which the earliest possible recognition is not only desirable but of the greatest importance in obtaining a satisfactory surgical result. This obstruction of the fourth ventricle has been observed at the author's clinic during the last four years in eight infants under six months of age.

Congenital obstruction of the fourth ventricle foramen should be suspected from the clinical appearance of the patient in the first months of life. The diagnosis can always be confirmed preoperatively by roentgenographic examination, including plain skull roentgenograms, ventricular air studies, and dural sinus venography. In this condition a huge cyst fills a much enlarged posterior fossa and projects downward into the cervical spinal canal as well as upward through the incisura of the tentorium. The tentorium fails to descend and is attached high on the parietal bones. There is obstructive internal hydrocephalus, which in some patients may be relieved completely by suboccipital craniectomy with excision of the cyst wall; in others it is converted to a communicating type of hydrocephalus, which must subsequently be treated by creation of a peritoneal or ureteral shunt. No surgical death occurred in the eight infants operated on at the author's clinic, but one patient died two months after operation with progressive communicating hydrocephalus complicated by convulsive seizures. Three of the remaining patients are doing well with no further treatment than wide excision of the cyst wall. In the other four patients excision of the posterior fossa cyst has had to be supplemented by spinal fluid shunting procedures to maintain normal intracranial pressure. The earliest possible recognition and definitive treatment of this lesion offers the best chance for a satisfactory result—and by satisfactory result is meant not survival, but opportunity for normal mental and motor development of the child.

Hemorrhagic Diathesis in Poliomyelitis. T. Bennike and L. C. Grandjean. Acta med. scandinav. 153:225-236 (No. 3) 1956 (In English) [Stockholm, Sweden].

Fifty-one (15%) of 349 severely paralyzed patients with poliomyelitis who were admitted to the Blegdams Hospital in Copenhagen, Denmark, during the 1952-1953 epidemic of poliomyelitis had a clinically manifest hemorrhagic diathesis in the form of bleeding into the skin, bleeding from mucous membranes and internal organs, and bleeding after tracheobronchial aspiration. The bleeding tendency was most pronounced in the most severely affected patients and occurred particularly within the first two weeks of the illness. Tracheobronchial hemorrhage predominated, but hematuria was also observed frequently. A systematic examination of 115 patients with poliomyelitis with varying degrees of paralysis revealed that 80% of the patients, irrespective of the presence or absence of a bleeding tendency, had abnormal capillary fragility. This persisted with little change for at least four or five months after the onset of the disease. These observations suggest that the hemorrhages were, at least in part, of vascular origin, since abnormal capillary fragility was the only regularly occurring defect in the hemostatic mechanism. The slow subsidence of the observed changes favors a neurogenic causation. An interplay may be considered between the reduced capillary resistance and one or more unknown factors, possibly resulting from the unphysiological state of many patients during the acute phase of the disease. The results of experiments in animals carried out by other workers suggest that the poliomyelitis infection may be associated with the occurrence of autoantibodies, possibly caused by the destruction of tissue resulting from the infection, which may have a harmful effect on the capillary wall.

PEDIATRICS

Congenital Nonhemolytic Jaundice with Disease of the Central Nervous System. I. M. Rosenthal, H. J. Zimmerman and N. Hardy. Pediatrics 18:378-386 (Sept.) 1956 [Springfield, Ill.].

The authors describe a case of persistent severe jaundice and progressive neurological disease in a 5-year-old boy. The neurological symptoms did not appear until he was 3 years old, although the jaundice was first noted when he was 2 days old. The condition was either the same as or closely related to the "congenital nonhemolytic jaundice with kernicterus," recently described by Crigler and Najjar in eight members of a single large family, although the patient was not a blood relative of this family. The jaundice observed in this condition is the result of the reduced capacity of the liver cells to metabolize and excrete bilirubin, but the pathophysiological mechanism remains obscure. The neurological syndrome consisted of staggering gait, slow and scanning speech, and an intention tremor. An electroencephalogram revealed irregular high voltage, 5 to 8 per second activity with some 3 to 5 per second activity in all areas. Atypical irregular sleep frequencies with a few suggestive discharges were present in the temporal areas. The neurological syndrome is believed to be the result of bilirubin encephalopathy. The authors prefer to use this term to signify damage to the central nervous system resulting from the toxic effects of bilirubin on the brain, and they believe the term "kernicterus" should be restricted to the pathological findings of pigmentation of the basal nuclei.

At laparotomy the patient's liver and gallbladder appeared normal, and the extrahepatic biliary system was patent. Biopsy of the liver was performed, and sections showed that the parenchymal cells were essentially normal. There was some vacuolization of many nuclei. No bile pigment was detected within the cells. In the portal areas, around the central veins, and occasionally between the liver cords were small foci of inflammatory cells. The patient made a good recovery from the operation. He has become able to walk a short distance unaided, but with a markedly ataxic gait. However, he is no longer able to feed himself. The course of this patient indicates that development of bilirubin encephalopathy is not necessarily confined to infancy. It can, apparently, occur in young children, and probably in older children and adults, if the concentrations of indirect-reacting bilirubin in the serum are sufficiently high for a prolonged period.

Transient Dysproteinemia in Infants, a New Syndrome: I. Clinical Studies. R. A. Ulstrom, N. J. Smith and E. M. Heimlich. A. M. A. J. Dis. Child. 92:219-233 (Sept.) 1956 [Chicago].

Four infants under 8 months of age with an unusual syndrome of edema, irritability, and pallor were studied during an 18-month period. All four were born at term, had had an optimal diet, and had no laboratory evidence of renal or hepatic disease. Marked hypoproteinemia was present in each patient at some time during the illness. The age of onset of symptoms ranged from less than 1 month to 7 months. The disease was apparently self-limited, with spontaneous recovery occurring in each infant between the 7th and 9th months of life. The striking similarity of the clinical findings in these patients suggests a single disease process. The extensive studies reported here seem to indicate that an abnormality in protein metabolism at the cellular level is responsible. The normal dietary intakes during the development of anemia and hypoproteinemia and the spontaneous return to normal without recognizable changes in the diet, as well as the many studies presented here, indicate that this disturbance was not primarily of dietary origin. The evidence at hand does not permit assignment of a definite etiological factor, although the mechanism for the development of signs and symptoms seems clear.

DERMATOLOGY

Malignant Blue Nevus. E. R. Fisher. A.M.A. Arch. Dermat. 74:227-231 (Sept.) 1956 [Chicago].

A 27-year-old white man first noticed a pinhead-sized blue nodule in the right occipital region of the scalp at the age of 17. Four years later he noted a progressive enlargement of the lesion and a mass in the right cervical region. Biopsy of the latter revealed a secondary malignant melanoma within a lymph node. The pigmented lesion of the scalp was excised, and a radical dissection of the right cervical lymph nodes was performed. The patient remained in good health during the next six years, but three months before hospitalization he noted a 20-lb. weight loss and numerous pigmented and nonpigmented nodules on the skin of the neck, back, and abdomen. There was weakness, anorexia, and moderately severe pain in the right upper abdominal quadrant. Examination revealed the liver to be enlarged and nodular. In addition to the cutaneous nodules, which varied in size from several millimeters to 1 cm. in cross diameter, several lymph nodes in the posterior cervical chain on the right were also palpably enlarged.

A needle biopsy of the liver was performed, and one of the subcutaneous nodules was excised. The clinical and morphological features of the malignant melanoma removed from this patient's scalp indicate its origin from a blue nevus. The vacuolation of the tumor cells, carcinomatous configuration, and nuclear pleomorphism and occasional mitotic figures are considered diagnostic of malignancy in lesions presenting other features of the blue nevus. It is interesting to note that the morphological appearance of the metastatic lesions in the subcutaneous tissue and liver did not possess features that would enable one to establish their derivation from the blue nevus. The tumor cells were spindle-shaped, without vacuolation, and resembled other malignant melanomas not arising in blue nevus. The vacuolation of the tumor cells observed is not unlike the change noted in the tumor cells of some melanomas during pregnancy. Such cytological alteration suggests a hormonal influence upon the tumor cells of this lesion, although this patient did not reveal any overt clinical manifestations of endocrine imbalance. The significance and nature of the asteroid bodies observed within the cytoplasm of some of the tumor cells of the present malignant blue nevus are not apparent. As far as the author was able to ascertain, such structures have not previously been recorded in pigmented tumors of the nevus-melanoma type.

Necrobiosis Lipoidica: A Disease of Changing Concepts. J. Graham Smith Jr. A.M.A. Arch. Dermat. 74:280-285 (Sept.) 1956 [Chicago].

The author analyzed the records of 19 patients with necrobiosis lipoidica seen at Duke Hospital. Data obtained on these 19 patients were compared with tabulated data from 34 of a total of 52 cases of necrobiosis lipoidica reported in the *A.M.A. Archives of Dermatology and Syphilology* during the past 10 years. Regarding the 19 cases, he says that in only one-fourth of these was necrobiosis lipoidica associated with diabetes mellitus even when patients with equivocal but not definitely diabetic glucose-tolerance curves were included in the diabetic group. When diabetes mellitus is associated with necrobiosis lipoidica, the diabetes mellitus usually develops first; however, the association of diabetes mellitus apparently does not alter significantly the age of onset for necrobiosis lipoidica. In reviewing the slides from 13 of the 19 patients, it was found that in only 4 of the 13 did there seem to be a resemblance to granuloma annulare, and so the author concludes that necrobiosis is probably not a variant of granuloma annulare.

Approximately 90% of cases of necrobiosis lipoidica occur in women; the Negro and Oriental races are rarely affected if at all, and the disease, while more commonly having its onset in young adults, occurs in all age groups except in infancy and early childhood. Lesions are not frequently seen in locations other than the lower extremities. Ulceration probably occurs more frequently in diabetics, but it may occur in nondiabetics. Mucous membrane lesions do not occur. The etiology of necrobiosis lipoidica is obscure, but the pathological changes are probably secondary to vascular abnormalities. Surgical excision with grafting if necessary to close large defects is the most effective therapy available at present. Intralesional injection of hydrocortisone deserves further trial.

Nickel Dermatitis. H. T. H. Wilson. Practitioner 177:303-308 (Sept.) 1956 [London, England].

This report is concerned with dermatitis resulting from contact with nickel or nickel-plated articles. Nickel-plated articles, such as the metallic parts of garters, are nearly always barrel plated: that is to say, they are nickel plated in an acid nickel solution in a rotating barrel. The thickness of nickel deposited is usually of the order of 0.0002 in. (0.05 mm.). When the plating process is complete, the articles are washed in hot water. Unless the washing is adequate, the plated articles are likely to become coated with a thin film of nickel salts. This may account for the fact that dermatitis often seems to develop for the first time soon after the wearing of a comparatively new nickel-plated buckle or clasp. In the present series of 85 women, 12 out of 22 stated that their dermatitis arose beneath a nickel-plated article purchased a month or less previously. The rash began as a localized dermatitis, usually at the back of the thighs, at the point of contact with the garter buckles. Less frequently it began under a wrist watch, necklace clasp, or earring. Swelling and redness of the eyelids sometimes preceded all other symptoms, and occasionally a chronic papular eruption developed on the elbow flexures or axillary folds before the onset of lesions elsewhere. In only two patients did the rash remain localized to a single area. In the remainder, after a few weeks or months, eczematous patches developed on other parts of the body. Nickel dermatitis appears to consist of two separate components: a simple dermatitis localized to the area of nickel contact, and a chronic eczema or neurodermatitis having no obvious connection with such contact. These two components are so intimately associated that the diagnosis of suspender dermatitis can often be made on seeing the characteristic papular rash on the patient's elbow flexures.

All patients were patch-tested against metallic nickel and solutions of nickel sulfate. In every case strongly positive reactions were observed to nickel sulfate (2.5%), and severe reactions fol-

lowed the few tests made with higher concentrations. It would appear from serial tests that a 1% solution is a suitable strength for patch testing and solutions stronger than 2.5% should not be used. Metallic nickel gave a reaction equal to 0.5 or 1% of the solution. Complete removal of all metal clasps and buckles did not suffice to prevent relapses in every case. Nickel sensitivity, once acquired, is likely to persist.

INDUSTRIAL MEDICINE

Silage Gas Poisoning: Nitrogen Dioxide Pneumonia, a New Disease in Agricultural Workers. R. R. Grayson. Ann. Int. Med. 45:393-408 (Sept.) 1956 [Lancaster, Pa.].

Two patients with acute respiratory disease due to inhalation of silage gas were observed by the author in August, 1954. One died. A thorough investigation of these two cases and of the silage gas that caused the illness indicates that the disease was caused by the oxides of nitrogen and is essentially a diffuse chemical bronchopneumonia caused by the irritating action of nitrous and nitric acids on the respiratory tree. The disease may be mild or severe, depending upon the degree of exposure. Nitrogen dioxide pneumonia has been described many times in industrial toxicology but has apparently not been previously described in the medical literature as due to inhalation of gases from ensilage. Special studies carried out on the corn ensilage and on the actual gas from the silo in which the two patients were poisoned proved that there was a poisonous concentration of the oxides of nitrogen. This condition was due to a combination of drought, high-nitrate soils, and an unventilated silo. Other studies demonstrated the toxicity of the actual gas and of experimentally produced gas from the same ensilage. Silage gas poisoning due to the oxides of nitrogen with the production of chemical pneumonia is a disease that probably occurs more commonly than is recognized. Physicians in rural areas should be aware of the possibility of this disease during summer periods when corn is being placed in silos, particularly during times of drought. No specific treatment is known for the resulting bronchopneumonia. Research should be directed toward the discovery of a specific therapy.

PATHOLOGY

Cushing's Syndrome in Children Associated with Adrenal Cortical Carcinoma: A Case Report with Review of the Literature. G. H. Guin and E. F. Gilbert. A. M. A. J. Dis. Child. 92:297-307 (Sept.) 1956 [Chicago].

A 3-month-old girl was admitted to the Children's Hospital of the District of Columbia because of obesity beginning 6 weeks before admission. For three weeks before admission the patient was noted to have an eczematoid and acne-form rash on the cheeks. The infant was obese, showing a buffalo hump and moon face. There was no axillary or pubic hair and no abnormality of the external genitalia other than slight clitoral hypertrophy. There was hirsutism of the upper lip and an erythematous papular rash over the face and neck. The abdomen was distended, and the liver was palpable. A firm mass unattached to the liver was palpated to the right of the umbilicus. X-ray examination revealed marked osteoporosis of the entire skeletal system. Exploratory laparotomy revealed a tumor replacing the right adrenal, which was removed. The infant died on the fourth postoperative day after several episodes of apnea. Examination of the surgical specimen established the diagnosis of cortical carcinoma of the right adrenal.

Twenty-eight cases of adrenal cortical carcinoma associated with Cushing's syndrome in children under 14 years of age were collected from the literature. The reported case is believed to concern the youngest patient with adrenal cortical carcinoma on record. The fact that the mother of this infant had diabetes is considered to be of special interest. Of the 29 tabulated cases, 20 occurred in females and 9 in males. Eighteen patients died, and all but one of these came to autopsy. Histological confirmation of adrenal cortical carcinoma in this patient had been obtained surgically. Nine patients underwent surgical treatment. Persistent elevations of plasma and urinary 17-hydroxycorticosteroids and urinary 17-ketosteroids after ACTH stimulation provide an additional aid for the diagnosis of adrenocortical carcinoma.

THERAPEUTICS

Hydergine (a Vasodilator): Clinical Report on Hydergine in Peripheral Vascular Disease. W. deHaven Stick. Pennsylvania M. J. 59:1072-1074 (Sept.) 1956 [Harrisburg, Pa.].

Having found that vasodilating agents such as tetraethylammonium chloride, Priscoline, and Ilidar phosphate were inadequate in the treatment of functional or organic occlusive vascular disease of the lower extremities, the author tried hydergine, an equiproportional mixture of the three hydrogenated alkaloids of the "ergotoxine group," namely, ergocristine, ergocornine, and ergokryptine. Nearly 2000 oral and 200 parenteral doses of hydergine have been given in the course of the last six months to about 20 patients at the New York Hospital. The majority of these patients with arteriosclerotic obstructive vascular disease were in the 55 to 75 year age group. Pallor, atrophy, reduced temperature, cyanosis, intermittent claudication, early digital necrosis, nocturnal ischemia, and frank gangrene of one or more digits were the characteristic symptoms. The drug was also given to a few patients with functional obstruction as seen in association with thrombophlebitis, phlebothrombosis, hyperhidrosis, and, in one patient, frostbite residuum. All routes of drug administration were utilized in nearly every patient, including the oral, sublingual, parenteral, and direct intra-arterial routes. The drug was given to each patient for at least six days.

Only five patients obtained palliative benefit from treatment with hydergine, and only one patient showed actual progress in healing. Hydergine with Ilidar may be indicated in acutely painful ischemia of the lower limbs as a preliminary or adjunct to surgical treatment. Hydergine, given intravenously, appears to be a drug of choice in coping with acute hypertensive phenomena precipitated by the injection of radiographic substances for diagnostic procedures. Medical sympathectomy by the use of vasodilating agents, including hydergine, is of slight value in the management of peripheral vascular disease. Surgical sympathectomy remains the method of choice when warranted.

The Combination of Reserpine with Methyl-Phenyl-Piperidine Acetate in the Treatment of Hypertension. G. Visco. Clin. terap. 11:11-32 (July) 1956 (In Italian) [Rome, Italy].

Reserpine has several side-effects and is ineffective in many types of hypertension. Methyl-phenyl-piperidine acetate (A. M. F. P.) has a central sympathomimetic stimulant effect and a mild sympathicoperipheral effect. A combination of the two drugs was used in the treatment of 23 patients with hypertension who were followed for from 1 to 14 months after the treatment. They were between 18 and 73 years of age (average age, 49.8 years). Eighteen patients had essential hypertension, 3 had malignant hypertension, and 2 had chronic nephritis in a preuremic state. Ten patients (43.4%) showed a great reduction in the pressure values. The decrease in the systolic pressure was marked; the decrease in the diastolic pressure was less marked but more constant. A. M. F. P. did not interfere with the hypotensive effect of reserpine, but did prevent its side-effects: drowsiness, asthenia, psychic torpor, and vertigo. Bradycardia, nasal congestion, and hypothermia were also somewhat checked with the use of A. M. F. P. The collateral effects, such as the increase in the appetite and body weight, were less marked but still very significant. The two drugs had a synergistic effect on the patients' euphoria and the incidence of tremor, diarrhea, and night dreams.

In another experiment the authors gave a dose of 15 mg. per day of A. M. F. P. to 13 patients who were being treated with high doses of reserpine. The effects of A. M. F. P. on side-effects were less evident: 10 of the 13 patients had bradycardia, 9 had asthenia and mental torpor, and 7 had nasal stuffiness. Treatment had to be discontinued in 4 patients who were receiving the drug by intramuscular injection.

Severe Hypoglycemic Reactions in the Course of Treatment of Diabetes Mellitus with Carbutamide (BZ-55). E. Bendfeldt and H. Otto. München. med. Wchnschr. 98:1136-1137 (Aug. 31) 1956 (In German) [Munich, Germany].

Severe hypoglycemic reactions to carbutamide (BZ-55) occurred in 2 of 740 patients with diabetes mellitus who were treated with this drug. The patients were adipose women aged 59 and 70 years who were given 5 tablets of the drug on the first

day of the treatment, 4 tablets on the second day, 3 tablets on the third day, and 2 tablets on successive days. In the younger patient, who had hypertension, cardiac decompensation, and diabetic nephropathy and who had been treated with insulin for many years, the fasting blood sugar level varied between 230 and 310 mg. per 100 cc. before the institution of carbutamide therapy; it dropped to 105 mg. per 100 cc. on the 10th day of treatment, when drowsiness and a mild right facial paresis occurred. In the evening of the same day the patient became unconscious and the blood sugar level dropped to 35 mg. per 100 cc. The patient became conscious within a few minutes after the intravenous administration of 40 gm. of dextrose (in 50% solution), and the neurological symptoms disappeared completely. Despite the administration of carbohydrates, the blood sugar level still bordered on hypoglycemia 27 hours after the last carbutamide tablet had been given. In the older patient, who had severe general atherosclerosis and who had been admitted to hospital for sclerotic gangrene in the right foot, the presence of diabetes mellitus had not previously been recognized, but the blood sugar level on admission was found to vary between 177 and 242 mg. per 100 cc. On the third day of carbutamide therapy the fasting blood sugar level had dropped to 90 mg. per 100 cc., when the patient became drowsy, confused, and finally unconscious with rattling breathing. An apoplectic attack was considered and the patient was given aminophylline and 10 gm. of dextrose, and after that her responsiveness was somewhat improved. The diagnosis of a hypoglycemic reaction was established by the determination of a blood sugar level of 70 mg. per 100 cc. Consciousness was restored completely after the intravenous administration of an additional 25 gm. of dextrose, but five hours later she again became unconscious. Consciousness was restored once more by the intravenous administration of 25 gm. of dextrose, and after that she was given 15 gm. dextrose orally every hour.

In these two patients, the insidious and protracted course of the condition and the central nervous manifestations, which dominated the clinical picture and which subsided within a short time after the intravenous administration of dextrose, reminded one of hypoglycemic shock after the administration of long-acting insulin. Both patients had other diseases in addition to diabetes. Preuremia with residual nitrogen values of 80 mg. per 100 cc. was present at the onset of hypoglycemia in both patients. Determinations of carbutamide in the blood and urine of the older of the two patients showed that the carbutamide blood concentration was within the usual limits 24 hours after the onset of hypoglycemia and that the carbutamide excretion in the urine was not reduced as compared with that in patients without renal impairment who had received the same dose of the drug. These findings suggest that at least in this patient renal impairment did not inhibit the excretion of carbutamide in the urine and, therefore, did not cause an accumulation of the drug in the blood that could have been responsible for the hypoglycemia. Patients with diabetes of long duration associated with severe late complications, as in the younger woman, may have a tendency to pronounced variations in their blood sugar level, and hypoglycemia may result from insignificant causes.

RADIOLOGY

Carcinoma of the Lip. P. M. Burke and F. S. Hopkins. New England J. Med. 253:552-555 (Sept. 20) 1956 [Boston].

During the 12-year period from 1938 through 1950, 225 patients with cancer of the lip were seen in the cancer section of the Westfield State Sanatorium. This report is based on an analysis of the 182 patients who received their primary treatment at this institution. All lesions were histologically proved squamous-cell carcinoma, and all patients have been followed for over five years. All except 6 of the 182 patients were men. Treatment consisted of surgical removal of the tumor in 69 patients, while 97 patients received only irradiation treatment and 16 received a combination of surgical and x-ray therapy. One hundred eighteen (65%) of the 182 patients survived for five years without recurrence. The five-year survival rate is 80% when it is adjusted for the 35 patients who died within five years of other causes without recurrence of cancer. This compares well with the five-year cure rate reported by others. There is considerable difference of opinion in the literature about the best method of treating the primary lesion. Surgical therapy is favored by some and irradiation by others. The authors found that primary lip cancers comparable in size and histological grade respond about as well to x-ray as to surgical therapy. When an enlarged lymph node is present, the extent of the neck dissection should be decided on an individual basis. Routine neck dissection for cancer of the lip without enlarged lymph nodes is not recommended.

Primary Chickenpox Pneumonia. D. Y. M. Tan, S. A. Kaufman and G. Levene. Am. J. Roentgenol. 76:527-532 (Sept.) 1956 [Springfield, Ill.].

It is not generally realized that the varicella virus is capable of producing such complications as pneumonia, encephalitis, and nephritis. Only 15 well-documented cases (including four fatal ones) of chickenpox pneumonia have appeared in the literature up to 1955. The authors present observations on 16 patients seen at the John Haynes Memorial of the Massachusetts Memorial Hospitals. Pneumonia as a complication of chickenpox occurred in adults over the age of 19 with one exception, a 5-year-old girl. The onset of the respiratory symptoms occurred within five days of the appearance of the rash. The rash was severe, and in most patients confluent over the whole body. Vesicles were also found in the mouth and pharynx. The patients were acutely ill, with temperatures of from 101 to 105 F (38 to 41 C). They had severe cough and several had hemoptysis. Half of them had chest pain and dyspnea. Physical examination of the chest was generally not remarkable despite the extensive roentgen changes. Three patients had generalized lymph-node enlargement. The white blood cell count was elevated in slightly less than half of the cases, but the differential count remained normal in all.

The roentgenologic changes showed a characteristic pattern. There were widespread nodular densities superimposed on increased bronchovascular markings. These infiltrates varied in size, and though some were sharply defined from the surrounding lung others seemed to merge with the adjacent tissue. Transitory changes were common, and the disease, in some cases, changed rapidly, some areas of infiltration resolving while others appeared. In a few instances there was a tendency for the nodules to coalesce so that there appeared to be patchy areas of consolidation. This was most noticeable ot the lung bases. No portion of the lung was spared, although the densities seemed heaviest about the hilum and gradually diminished toward the periphery. While an etiological diagnosis of pneumonia is not possible from the roentgenologic examination alone, it has been the experience of these authors that these striking findings in a patient with chickenpox can be taken as presumptive evidence of primary varicella pneumonia. This can usually be confirmed by clinical and laboratory findings. Various chemotherapeutic agents were tried without success, the disease varying in duration from a few days to two weeks. There were no fatalities.

Therapy of Dupuytren's Contracture. K. Wasserburger. Strahlentherapie 100:548-560 (No. 4) 1956 (In German) [Munich, Germany].

At the department for irradiation therapy of a Vienna Hospital efforts have been made to develop an effective radium therapy for Dupuytren's contracture. Radium therapy is carried out with an apparatus for distant therapy, which is a circular arrangement of eight barrel-shaped holders, each of which contains 50 mg. radium element. The 400 mg. of radium element are filtered through 1 mm. of platinum. Lateral shielding is provided by 4 cm. of lead. The instrument is mounted in such a way that the effective cone of rays can be directed and fixed in any desired position. The radium-skin distance in the treatment of Dupuytren's contracture was 2 cm. The size of the field of treatment was 5 sq. cm. Depending on the extent of the lesion and on whether one or several fingers was involved from three to five fields were irradiated on each hand. If necessary the series of treatments was repeated after from three to six months.

Irradiation treatment was applied to 213 patients with Dupuytren's contracture during the years from 1937 to 1953. The irradiation was the primary treatment in 185 of these patients, the remaining 28 having first received surgical treatment. Follow-up studies on 146 of the 185 patients revealed that in 102 the results were very good, 24 others obtained improvement, and the remaining 20 experienced no improvement.

In classifying the lesions according to the degree of severity and advancement, it was found that of the patients with stage 1 lesions, 89.8% were cured; of those with stage 2 lesions, 56.5%; and of those with stage 3 lesions, 32.2%. This indicates the importance of early treatment.

Angiocardiography in the Preoperative Diagnosis of Mitral Stenosis and Insufficiency. J. G. McAfee, T. F. Hilbish and K. R. Stewart. Radiology 67:321-331 (Sept.) 1956 [Syracuse, N. Y.].

The authors performed angiocardiography in 50 patients with mitral rheumatic heart disease, but this report is concerned only with the 32 surgically proved cases. Although the surgical correction of mitral stenosis has become firmly established, that of mitral regurgitation has remained largely experimental. In the preoperative evaluation of patients, therefore, the accurate differentiation of stenosis from insufficiency is of the utmost importance. Angiocardiography is not a reliable procedure for distinguishing between mitral stenosis and insufficiency. The diagnostic accuracy was poorer than that of conventional clinical methods. Both false-positive and false-negative diagnoses of mitral stenosis were made. In this, as in other unselected series, patients with stenosis predominated. The problem of selecting the small minority with predominant insufficiency has not been solved by angiocardiography. No difference in the "opacification pattern" of the left atrium and ventricle was observed in stenosis and insufficiency that could not be explained on the basis of chamber size and cardiac phase. The prolonged opacification of the left atrium seen in mitral disease is due to its large size and generalized slowing of the circulation. In the absence of shunts, the output (volume per unit time) in all chambers of the heart remains equal; there is no specific "hold-up" of the contrast medium in the left atrium by a stenotic mitral valve. Angiocardiography is of value in demonstrating the size and position of the cardiac chambers, but this can usually be assessed by ordinary roentgenographic means. Left ventricular enlargement was demonstrated in only two of five patients with proved "pure" mitral insufficiency. It may be possible in the future to visualize the mitral valve orifice by selective angiocardiography performed through a direct left atrial puncture.

Congenital Cystic Adenomatoid Malformation of the Lung in Infants. J. M. Craig, J. Kirkpatrick and E. B. D. Neuhauser. Am. J. Roentgenol. 76:516-526 (Sept.) 1956 [Springfield, Ill.].

Formation of cysts related to alveolar and interstitial emphysema is frequent in early life in infants suffering from neonatal asphyxia associated with the formation of hyaline membranes and in those with pneumonia, due to Streptococcus pyogenes. Cysts of this origin usually resorb quickly and without sequelae. Infants with indisputably congenital cystic malformations have been observed at the Children's Medical Center of Harvard University over the past 25 years, in whom the structure of the cystic lungs was such that it was inconceivable that they would ever function normally or that the cysts would disappear spontaneously. In the four cases reported, surgical extirpation was carried out in the first two weeks of life. They presented the identical features described by Ch'in and Tang as "congenital adenomatoid malformation." All four infants had similar signs and symptoms, consisting of cyanosis, rapid respirations, and an absence of respiratory distress or fever. The physical signs were those of displacement of the mediastinum to the side opposite that of the affected lung, dulness to percussion over the affected lung, and diminished breath sounds over this area. The roentgen signs in all four infants were those of an intrapulmonary mass of soft-tissue density, containing scattered radiolucent areas. The outlines of the mass were usually quite sharp and the malformation was limited to one lobe. A roentgenogram taken very early in life may show only the presence of a soft-tissue density without any radiolucent air-containing areas, at a time before any air has penetrated the honeycombed mass. At operation, the mass was usually well defined. The anatomy of the lesion is striking because of the great increase in size and weight of the affected portion, many of the affected lungs being twice the usual dimensions and weight.

Since in two of the infants the involved lungs increased rapidly in size with a concomitant increase in the air-containing cystic structures with further displacement of the mediastinum and compromise of respiratory function, it appears that once a definite diagnosis of such adenomatoid cystic malformations is made, surgical treatment is mandatory. It proved effective in three of the four infants, but the fourth infant died two days after the operation. Congenital cystic adenomatoid malformation should not be confused with either the accessory lung, which has no connection with the bronchial system or pulmonary blood supply, or with the sequestrated lobe, which is usually connected with the bronchial system but derives its blood supply from a branch of the aorta.

PHYSIOLOGY

A Comparison of the Biological Values of Dietary Protein Incorporated in High- and Low-Fat Diets. V. C. Metta and H. H. Mitchell. J. Nutrition 59:501-513 (Aug.) 1956 [Philadelphia].

The effect of fat as compared with that of isocaloric amounts of carbohydrate on nitrogen utilization in the severely protein-depleated and the growing rat was investigated. The low-fat and the high-fat diets contained, respectively, 5 and 33% fat, mainly lard. Casein was the dietary protein tested. The rats were fed the test diets so that they received equal amounts of protein, crude fiber, vitamins, minerals, and gross energy, the main difference between the two groups being in the fat intake. When fed in isocaloric amounts, dietary fat and carbohydrate had essentially the same effect on protein utilization in both the protein-depleted rat and the growing rat. Neither the apparent digestibility nor the true digestibility of casein was improved by the higher dietary fat level. Fat did not seem to spare endogenous nitrogen under conditions of satisfactory and equal caloric intake. Higher dietary fat levels did not improve the biological value of casein. In fact, the indications in one experiment were that a high-carbohydrate diet tends to improve the biological value of casein in the protein-depleted rat. The metabolic fecal nitrogen per gram of food intake increased significantly when the dietary fat was increased because of a concomitant reduction in the food intake due to isocaloric feeding. This value, however, remained constant irrespective of the fat content of the diet when the rats were fed equal amounts of the low-fat and the high-fat diets.

The Determination of Chromosomal Sex by Oral Smears. W. Herrmann and A. M. Davis. Yale J. Biol. & Med. 29:69-74 (Sept.) 1956 [New Haven, Conn.].

Oral smears were obtained from 100 persons of varying ages for a control series. Fifty men and 50 women each had the buccal mucosa scraped with a wooden spatula. The material obtained was smeared on a glass slide and immediately dropped into a solution containing equal parts of ether and 95% ethyl alcohol. The slides were then stained with the Papanicolaou stain. Each slide was studied under an oil immersion lens, and the sex chromatin was easily identified. The sex of the person from whom the specimen was obtained was not known until after the counts had been made.

The authors then applied the test to 15 patients whose true sex was questionable. Four of these patients had been given a clinical diagnosis of pseudohermaphroditism, three being considered anatomically female and one anatomically male. One of the three females had proved congenital adrenal hyperplasia, with a diagnosis confirmed by the elevated beta fraction of the 17-ketosteroids. The other two were newborn twins on whom no endocrine essays had as yet been performed. These twins showed a phallus-like development of the clitoris. All three patients had a female chromosomal pattern. The anatomically male pseudohermaphrodite was 44 years old and had previously been given a diagnosis of a male achondroplastic dwarf. A chromatin count indicated that this patient was genetically female. Two of the patients with gonadal dysgenesis proved to be chromosomally male, even though they had female genitalia and were living satisfactory lives emotionally, physically, and mentally as females. The true hermaphrodite had female external genitalia, a testis on one side and an ovary on the other, and a chromatin count following a female pattern. In the remaining cases the chromosomal sex corresponded with the anatomic sex.

BOOK REVIEWS

The Neurosurgical Alleviation of Parkinsonism. By Irving S. Cooper, M.D., Ph.D., F.A.C.S., Director, Department of Neurosurgery, St. Barnabas Hospital, New York City. Cloth. $8.50. Pp. 104, with 68 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

This book will undoubtedly be widely read. Unfortunately paralysis agitans is a widespread and disabling condition. As there has been no truly satisfactory treatment for this chronic disease, many of its victims will look hopefully to the possibility of relief that is held out here. One of the barriers to investigating this condition lies in the fact that the disease has never been produced in animals and cannot, therefore, be studied by investigations in laboratory animals. Observations regarding the condition, its cause, pathological physiology, and treatment, must be made on man himself. It is notoriously difficult or impossible to conduct human investigations with the same scientific care that can be exerted with the laboratory animal. This is all the more reason why observations on human beings should be even more painstakingly made than those in the experimental laboratory. Unfortunately this book and the material recorded here do not meet that requirement. One is struck by the lack of a critical approach and by the indifference with which essential detail is treated. Occlusion of the anterior choroidal artery (now largely or completely abandoned) and injection of alcohol into the general region of the globus pallidus are the two methods of treatment advocated by the author. These may be the forms of treatment that will ultimately prove the most satisfactory. The facts, however, that the globus pallidus is being injected in these cases, that it is destruction of the globus pallidus and not of some other structure in that general neighborhood that is responsible for the results reported here, or that these forms of treatment are capable of reversing even the most far-advanced, deforming, incapacitating signs and symptoms of paralysis agitans have certainly not been established here. Only much more time and far more meticulous study can determine the true worth of these procedures.

Proceedings of the International Conference on the Peaceful Uses of Atomic Energy Held in Geneva, 8 August–20 August 1955. Volume 10: Radioactive Isotopes and Nuclear Radiations in Medicine. Volume 11: Biological Effects of Radiation. United Nations Publications sales no. 1956. IX.1. Vol. 10; 1956. IX.1. Vol. 11. A/Conf. 8/10; A/Conf. 8/11. Cloth. 98; 57s.; 34 Swiss francs, each. Pp. 546; 405, with illustrations. United Nations, New York; Columbia University Press, 2960 Broadway, New York 27, 1956.

These two volumes, which in themselves are impressive in size and content, are parts of a monumental series of 16 that summarize the scientific work of the famous Geneva conference. Volume 10 is in four sections; the first of these is introductory, the second deals mainly with uses of radioactive isotopes in therapy, and the third and fourth deal with uses in diagnosis and research. The individual isotopes most frequently mentioned are strontium-90, cobalt-60, iodine-131, astatine-211 (which resembles iodine in being selectively accumulated by the thyroid gland but differs strikingly in emitting alpha instead of beta particles), phosphorus-32, hydrogen-3 (tritium, useful as the oxide in studies of water metabolism), rubidium-86 (useful as a tracer for potassium), carbon-14, and sulfur-35. A chapter on the therapeutic usefulness of radioactive colloids points out that gold-198 is the only isotope that can be used in this way. Phosphorus-32 in the form of chromic phosphate is a colloid, and the chlorides of yttrium-90 and lutetium-177 after injection form colloids in the body fluids. All four are beta-emitters, but they differ in half-life, energy of the particles emitted, presence or absence of gamma radiation, and hazards in handling and shipping. They afford an excellent illustration of the apparently inexhaustible possibilities opened up by the discovery of artificially induced radioactivity.

Volume 11 is in six sections that deal respectively with the general biological effects of radiation, radiation injuries, carcinogenic effects and the bone-seeking isotopes, reproductive effects, protection and recovery, and genetic effects. Many of the chapters have immediate technical value because they go into detail about therapeutic techniques such as the use of surface applicators, revolving cobalt-60 units, teletherapy, intracavitary injections, pellets, wires, and nylon ribbons. Of great general interest are five chapters that describe the acute radiation injuries among inhabitants of Hiroshima and Nagasaki in 1945, the subsequent chronic effects, the injuries to Japanese fishermen in 1954, the references and data regarding certain mishaps to Americans who were working around nuclear reactors, and case histories of two Russian workers who suffered a short general exposure to gamma and neutron radiation when rules for operating an experimental reactor were violated. It is quite difficult to locate particular topics in these volumes not only because an index is lacking but also because the order of chapters is that in which the papers were presented in Geneva rather than according to subject. The editing, however, has converted a maze of contributions from all parts of the world into a harmonious work. The mathematical parts are beautifully set up, the text is extraordinarily free from errors or ambiguities, there are good bibliographies with the various chapters, and the illustrations are excellent.

Ulcers of the Legs. By P. Piulachs, Chief Professor Surgeon in Faculty of Medicine of Barcelona. Cloth. $15.50. Pp. 574, with 303 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1956.

This well-written book is divided into sections entitled General Conceptions of Leg Ulcers, Ulcers of Venous Etiology, Physiopathology of Ulcers Due to Venous Insufficiency, New Pathogenetic Concept of Varicosities, Evolution of the Venous Thrombosis and of Its Sequelae, Arterial Ulcers, and Trophoneurotic Ulcers. The author makes a pertinent and simple distinction between ulcerations (which heal in a short time) and true ulcers (which are chronic and resistant to therapy). True ulcers are divided into three etiological types: arterial, venous, and neurotrophic. The chapter dealing with the physiopathology of ulcers is one of the best in the book. Much space is devoted to the influence of postural changes. The author believes that normal persons when standing are on the verge of peripheral edema. The roles played by the systemic circulation, venous valves in orthostasis, and contraction of abdominal muscles and the influence of muscular activities on the venous valves of the lower extremities are explained. Piulachs presents his own concept of the pathogenesis of varicosities, which stresses the importance of the existence of arteriovenous communications. In the section on the neurotrophic factor in vascular leg ulcers, he described his original studies on this subject. He clearly demonstrates the state of the capillaries around the ulcer by using capillaroscopic examinations. He believes that the best treatment of superficial incompetency is stripping of the saphenous vein. He presents his method of correcting deep venous insufficiency by interrupting an avascular column of deep venous blood. The text is clearly written on good paper and is profusely illustrated. This book is highly recommended.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Handbook of Legal Medicine. By Louis J. Regan, M.D., LL.B., Professor of Legal Medicine, University of Southern California, Los Angeles, and Alan R. Moritz, M.D., Professor of Pathology, Western Reserve University, Cleveland. Cloth. $3.90. Pp. 201, with 11 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

For many years the need in our medicolegal library for a short, simple, concise review of the many subjects referred to under the heading of medical jurisprudence and the various aspects of scientific medicolegal investigations has been recognized. In this book two of the outstanding experts in the United States have discussed these subjects in an understandable and acceptable form to medical and legal students. Unfortunately the average student of law or of medicine has had little or no opportunity to study these subjects during his regular academic schedule. When in the past the need arose or the desire existed to study in this field, the student has been discouraged by the voluminous and technical nature of published material. This obstacle has now been removed. The book will also provide a useful working manual for practicing lawyers and physicians. While it is true that for the few who are expert in these two fields the material presented will be elementary, for most lawyers and physicians, it will be a valuable and useful guide.

Dr. Regan tends to dicuss many subjects in terms of medical professional liability rather than in relation to the broader field of personal injury litigation. Although this approach may mislead some readers as to the importance or significance of some of the subject matter, it has not apparently resulted in any inaccuracies or misstatements. The second portion of the book should be of great value to students and physicians, but it should be particularly helpful to attorneys who are confronted with the investigation, prosecution, or defense of cases involving violent crimes or disputed paternity. This section of the book should provide them with a clear and authoritative commentary on the major aspects of these subjects. The book includes an extensive glossary of medical and legal terms, a detailed table of contents, and a bibliography of selected references in the medicolegal field. This book should be widely circulated not only for the education and edification of students, lawyers, and physicians but also as an important aid in the better administration of justice in civil and criminal cases.

Head Injuries and Their Management. By Francis Asbury Echlin, M.D., C.M., M.Sc., Professor Clinical Neurosurgery, New York University, Postgraduate Medical School, New York. This material was published in American Practitioner and Digest of Treatment for May, 1958. Cloth. $3. Pp. 127, with 10 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada; Pitman Medical Publishing Company, Ltd., Pitman House, 39-41 Parker St., Kingsway, London, W.C.2, England, 1958.

The book, which is small enough to slip into a coat pocket, is a brief description of the essentials in diagnosis and treatment of head injuries for residents and the practicing surgeon and physician. There are succinct chapters on the mechanisms of head injury, nonsurgical lesions of the brain, surgical conditions such as hematomas, scalp wounds, skull fractures, penetrating wounds of the brain, and a few paragraphs on infections and other complications, including post-traumatic epilepsy, cerebral palsy, the post-traumatic syndrome of headache, "dizziness" and nervousness, and neuroses, psychoses, and rehabilitation. Discussions of pneumography, angiography, and electroencephalography are so brief as to be of no particular value. A good selective bibliography and an adequate index conclude the volume. Within its limited aims, the volume contains no serious errors except those of omission. Precisely, it is a primer, of limited value for students, interns, and residents. There is nothing here for neurologists or neurosurgeons and nothing to equip a general surgeon for the surgical management of head injuries. It rightly points out that over 97% of closed head injuries require no operation and presents admirably the generally accepted criteria for diagnostic appraisal, observation, and management. As any primer must, it lacks important surgical details, and, even for so brief a manual, it is inadequate in its discussion of all the nonsurgical aspects of head injuries such as the post-traumatic syndrome, pneumography, angiography, and the electroencephalogram. No account is given of the medical treatment of post-traumatic convulsive states. Discussion of the post-traumatic neuroses and psychoses is passed over entirely. The book is thus grossly inadequate; perhaps any brief presentation of the problems of head injuries must be inadequate. To make the complex simple is a most dubious enterprise, as this book amply demonstrates.

Industrial Medicine and Hygiene. Volumes I-III. Edited by E. R. A. Merewether, C.B.E., O.St.J., M.D., H.M. Senior Medical Inspector of Factories, Ministry of Labour and National Service, [London, England.] With foreword by The Lord Horder, G.C.V.O., M.D., F.R.C.P. Cloth. Pp. 426, with 33 illustrations; 451, with 81 illustrations; 617, with 57 illustrations. F. A. Davis Company, 1914-1916 Cherry St., Philadelphia 3; Butterworth & Co., Ltd., 88 Kingsway, London, W.C.2, England; 1367 Danforth Ave., Toronto 6, Canada, 1954; 1956.

This is an ambitious work, as indicated by its title. It comprises three volumes, lists about 1,500 references to the pertinent European and American literature, and contains sections from over 30 contributors representing medicine, pharmacology, toxicology, chemistry, psychology, nursing, industrial hygiene, civil and electrical engineering, law, and management. Besides industrial medical directors and governmental plant inspectors, the physicians contributing include public health specialists, internists, ophthalmologists, otolaryngologists, dermatologists, and some who are lawyers as well. The first volume should be of particular value to the British reader, inasmuch as it presents the background and basis, in British history and law, of workmen's compensation and of programs of industrial health and rehabilitation and the organization and statistics of health services of various British industries. The American reader will derive greater profit from a study of the other two volumes. Volume II deals with occupational skin diseases, ophthalmology, psychology, compressed air, heating, ventilation, lighting, noise, ionizing radiation, and industrial accidents. It discusses the causes, prevention, and in some instances the treatment of harmful effects from these agents and influences. Volume III, far thicker than either of the other volumes, deals with silicosis and other pneumonoconioses, industrial carcinogenesis, and toxicology. It offers an exhaustive but, for the average physician, somewhat hard-to-understand account of the chemistry, enzyme reactions, and derangements involved in the various industrial intoxications. This work is well written. It is an authentic source of valuable information; guidance, especially for the British; and references, particularly on industrial and compensation medicine, rehabilitation, toxicology, and, to a lesser extent, industrial hygiene.

British Postgraduate Medical Federation, University of London, Lectures on the Scientific Basis of Medicine. Volume IV: 1954-55. Cloth. $6.50. Pp. 397, with 34 plates. Athlone Press, University of London, 2 Gower St., London, W.C.1, England, John de Graff, Inc., 31 E. 10th St., New York 3, 1956.

This volume contains 21 lectures, most of them very interesting, on a variety of medical subjects; each is by a different speaker. It will probably be most appreciated by medical students as a book to be picked up from time to time to furnish inspiring sidelights on anatomy, biochemistry, and physiology. A chapter on the chemistry of the porphyrias, for instance, includes photographs showing the devastating physical effects of this metabolic disease. A chapter on nucleoproteins in cell structure shows how the ability of these complicated, three-dimensional molecules to duplicate themselves is involved in most processes of growth and reproduction. A chapter on the cooling of the whole organism gives recent results on artificial hibernation, considers the danger and prevention of cardiac fibrillation in hypothermia, and sketches possible applications in surgery. The chapter on alcohol contains much scientific information enlivened by a discreet

touch of humor. Other topics that will appeal to the medical student include the chemical aspects of abnormal growth, shock from burns, radiation injury to bones, and the effects of distention of viscera. The book also offers chapters that will be especially appreciated by physicians seeking coherent summaries of recent developments in the basic sciences; some of these chapters are entitled The Plasma Proteins, Laboratory and Clinical Findings in Hypersensitivity, Reaction of Enzymes to Injury, and Fat Metabolism. The book lacks an index, but each chapter includes a bibliography. The illustrations are excellent.

The Practice of Psychosomatic Medicine as Illustrated in Allergy. By Hyman Miller, M.D., Associate Clinical Professor of Medicine, University of California at Los Angeles, Los Angeles, and Dorothy W. Baruch, Ph.D. Cloth. $5. Pp. 196. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C. 4, England, 1950.

This book, written by an allergist and psychologist, is mistitled, for it is not a treatise on the practice of psychosomatic medicine but rather a monograph on the psychosomatic approach to allergy. Its focus is on allergic patients, and, although much significant information is contained about the role of the psyche in the sufferings of such patients, general applications for the whole field are not discussed. The authors contend that the allergic patient, like any sick person, can only be understood in the context of his total family situation. Both the allergic constitution and the emotional climate of the family are significant in the production of the disease. Emotional factors act as trigger mechanisms for the production of the symptoms. The task of diagnosing these factors in adults and children requires special technical procedure, and their treatment is effected by means of special skills not transmitted through reading. The book is simply written and easily understandable. The authors recognize that emotional factors are but a part of the total allergic syndrome, and this part they present well. Reading the book may stimulate allergists to obtain more training in psychodynamics or to greater willingness for cooperation with psychiatrists. The bibliography and index are barely adequate.

Surgical Forum. Volume VI. Proceedings of Forum Sessions, Forty-First Clinical Congress of the American College of Surgeons, Chicago, Illinois, November, 1955. Surgical Forum Committee; Harris B. Shumacker, Jr., chairman, and others. Cloth. $5. Pp. 654, with illustrations. American College of Surgeons, 40 E. Erie St., Chicago 11, 1956.

Beginning with this volume, the American College of Surgeons has itself assumed responsibility for publication of the annual "Surgical Forum." The contributions cover the fields of general surgery, neurosurgery, gynecology and obstetrics, orthopedics, plastic surgery, and urology. The contents of the volume reflect most of the advances in these fields and point toward further studies in clinical surgery. The printing, binding, and illustrations are of the same excellence that characterized the previous volumes.

Joint Ligament Relaxation Treated by Fibro-Osseous Proliferation. By George Stuart Hackett, M.D., F.A.C.S., Consulting Surgeon, Mercy Hospital, Canton, Ohio. With special reference to low back disability—trigger point pain and referred pain. Cloth. $4.75. Pp. 97, with 17 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

This monograph propounds the theory that most backache and pain in or about other joints is due to chronic relaxation of ligaments. While it is true that chronic relaxation of ligaments may and does at times produce localized and referred pain, such as the author has described and treated by his method of injection, there are many other conditions, such as fibrositis, bursitis, or chronic edema at the insertion of ligaments or tendons, that frequently cause local soreness and referred pain. Although it may not be possible to agree with the author that the cause of localized tenderness and referred pain is mainly relaxation of ligaments, the treatment he advocates is logical for many of the conditions that produce backache with referred pain. Many orthopedists have found the use of a local anesthetic for the injection of "trigger points," with or without the added injection of other substances such as hydrocortisone or a mild irritant, to be helpful in relieving this painful syndrome. This is an interesting and challenging book, but some of the statements found in it will not be accepted by most orthopedists. The report of such a high incidence of recovery of the patients treated by the author should cause all physicians whose minds are not closed to new ideas to study the methods used and put them to the therapeutic test.

Ciba Foundation Colloquia on Endocrinology. Volume 9: Internal Secretions of the Pancreas. Editors for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., and Cecilia M. O'Connor, B.Sc. Cloth. $7. Pp. 292, with 100 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, England, 1956.

The present colloquium is a follow-up of a previous one dealing with carbohydrate metabolism that was held by the Ciba Foundation in 1952. A group of American and European workers reviewed their recent experimental studies in this field. Their reports as well as the discussions that followed each report summarize most of the research that is now being conducted. The subjects treated are the effects of agents that specifically alter the alpha cells of the pancreas, glucagon, the chemical structure and configuration of insulin, the permeability of cells to glucose and other sugars, the hepatic actions of insulin, and the interactions of pituitary growth hormone and insulin in the organism. Since the book deals primarily with animal experiments, it will be of primary interest to the research worker rather than to the clinician. The demonstration, however, that destruction of the islet tissue affects carbohydrate metabolism quite differently than does pancreatectomy and the observed actions of the hyperglycemic glycogenolytic factor of the alpha cells may alter radically our present notions of the pancreas and carbohydrate metabolism and may have practical clinical significance. As with the other volumes in this series, the editors and publishers have produced a well-written and excellently printed book.

Fluid Balance Handbook for Practitioners. By William D. Snively, Jr., M.D., Attending Physician, Evansville Child Health Clinics, and Michael J. Sweeney, M.D., Attending Physician, Evansville Child Health Clinics, Evansville, Ind. Cloth. $6.75. Pp. 326, with illustrations by Kathleen Calhoun. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

This is an exceedingly well-written book by two authors who are well qualified to discuss this subject. They have presented all the problems of fluid imbalance in a simple logical fashion. The types and composition of body fluids and their shifts are specifically discussed. Electrolyte imbalance and all the clinical problems of acid-base equilibrium are included, and the methods of handling these problems are discussed. Specific instructions for determining amounts, kind, and rate of fluids are suggested by a simple set of rules. There are actual case problems presented at the end of the book as exercises for handling specific imbalances. This small volume can be read in a few hours. The format is pleasing, and the illustrations, figures, and tables are excellent. The bibliography is rather scant. This book can be recommended to all students and to practioners of medicine and surgery who are confronted with problems of fluid imbalance.

Textbook of Urology. By Victor F. Marshall, M.D., F.A.C.S., Associate Professor of Clinical Surgery (Urology), Cornell University Medical College, New York City. Cloth. $5.50. Pp. 268, with 66 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1956.

This book represents a needed concise, accurate urologic textbook. The contents are well arranged and presented in a straightforward manner. The urologic concepts are those current in the field of diagnosis and treatment. The diagrammatic representation of urologic disease as a pyramid leading to a cure is clever. The base of that pyramid is an adequate history and physical examination, tools available to all interested physicians. The text reads easily and is occasionally interspersed with appropriate comments. This book is recommended for medical students and practicing physicians.

QUERIES AND MINOR NOTES

LIGHTNING PAINS

To the Editor:—*A 42-year-old man contracted syphilis in 1938, after which he had a course of treatment of bismuth and mercury. This course was completed in 1944, and since then he has had penicillin ranging up to 6 million units. The primary symptom at present is apparently that of a neuritic pain largely involving the knees. X-ray revealed no evidence of syphilitic involvement, and neurological examination is negative. He has a persistently positive reaction to the Wassermann, Mazzini, and Venereal Disease Research Laboratory tests. The pain this man is experiencing can be dulled with aspirin, Empirin, or Demerol, but not completely relieved. Otherwise he is in good health and is able to work in the oil fields regularly. What course of treatment might be available for prevention of the pain or at least a check of its frequency?*

M.D., Montana.

Answer.—The information provided is inadequate to permit an opinion as to whether the neuritic pain primarily involving the knees is or is not potentially associated with the patient's long-standing syphilitic infection. So-called neuritic pains in patients with late syphilis are practically always characteristically lightning or lancinating in character. The character of the pain is sharp, stabbing, and knife-like, each individual pain lasting only for a second or a fraction thereof. These pains tend usually to occur in the lower extremities and are characterized by the fact that they shift from one place to another, sometimes in a toe or sometimes in the ankle, the calf, the knee, or the thigh. They tend to occur in attacks of varying severity, ranging from minor inconvenience that is readily relieved by a mild analgesic, such as aspirin, up to attacks of agonizing severity that may require large doses of morphine or other powerful analgesics. The individual attack of pain may last for an hour or two only or may continue for days at a time. In most cases, the attack ceases either spontaneously or after administration of analgesic drugs, and the patient is completely free from discomfort in the interval between the attacks. This interval may vary from days or weeks to months. An extraordinary feature of this type of pain is that the attacks may be precipitated or triggered by several widely varied circumstances, including a change in the weather, an elevation of body temperature, the presence of focal infection, fatigue—whether physical or mental—and constipation. The attacks are only occasionally completely relieved by any form of antisyphilitic therapy, whether metal or antibiotic chemotherapy, though some patients may obtain partial relief in terms of lessened frequency and severity of attacks.

The diagnosis of lightning pains depends entirely on the patient's description of his subjective discomfort, plus, in most cases, associated neurological evidence of tabes dorsalis. The pains are due to involvement of the posterior roots and columns of the spinal cord and may constitute the earliest symptom of tabes, appearing before there are objective evidences of neurological damage. Pains of this nature do not occur in any other condition. If the patient's pain is of the nature described, it seems reasonably certain that it is due to the old syphilitic infection and that confirmation of this may be had either by very careful neurological examination, with particular reference to objective evidence of damage to posterior columns of the spinal cord, and/or by examination of the cerebrospinal fluid, which does not appear to have been done. The management and treatment of lightning pains often call for the highest skill in the art of medicine, with many ancillary factors to be considered other than antisyphilitic treatment itself. In this particular patient, if the neuritic pain does not conform to the description given above, it is highly improbable that these pains have anything to do with syphilis.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

TOXICITY OF 2,4-DICHLOROPHENOXYACETIC ACID (WEED SPRAY)

To the Editor:—*A farmer who has been perfectly well began using 2,4-dichlorophenoxyacetic acid (2,4-D) to spray weeds several weeks ago. He inhaled considerable spray, after which he had a burning sensation in the throat and chest, became weak, and lost his appetite and some weight. Examination of the urine revealed nothing except 2+ albumin, with no casts or blood cells. On discontinuing use of the spray, he gradually improved and the urine has cleared up. This trouble came on also last year and the year before when he used the same spray. On two occasions, he had two other men helping him, both of whom became ill in a similar manner, requiring several weeks for recovery. In the July 18, 1953, issue of* The Journal, *page 1144, the following statement appeared in an editorial "Relief from Ragweed": "2,4-D is comparatively harmless to animals and humans." The article also states that "the dusts of 2,4-D can be irritating to the eyes and respiratory tract," but no reactions were mentioned that were as severe as apparently occurred in these people. Could this illness be due to inhalation of 2,4-D?*

W. E. Wilson, M.D., Northfield, Minn.

Answer.—All available evidence tends to indicate that the sodium salt of 2,4-D is relatively nontoxic when wet or dry clouds are inhaled. Animal experiments with this material did not produce any evidence of lung irritation; however, in concentrated form it is likely to be irritating. The oral $L. D._{50}$ for mice is about 280 mg. per kilogram. Injection of 150 to 200 mg. per kilogram produced myotonia followed by sluggishness and shallow respiration in mice. There is a possibility of individual sensitivity to 2,4-D in persons susceptible to phenol compounds; 2,4-D formulations contain petroleum distillates that may cause varying degrees of discomfort. This factor should be taken into consideration in complaints after exposure to this class of herbicides.

SIDE-EFFECTS OF RADIOTHERAPY

To the Editor:—*Has the value of nicotinamide been scientifically demonstrated for the prevention of the side-effects of radiotherapy? In the city, most of the radiologists routinely prescribe liver extracts and/or vitamin B_{12} for patients exposed to x-rays to prevent postradiotherapeutic leukopenia and anemia. This practice seems illogical, particularly in leukemias and allied disorders, because well-conducted radiotherapy is likely to relieve a preexisting anemia and not aggravate it and these substances probably further the development of the leukemic cells. Are these assumptions correct? What about the use of glutathione, cysteine, thymonucleic acid, and cortisone to prevent the side-effect of radiotherapy?*

Jacques Messerschmitt, M.D., Algiers, Algeria.

Answer.—There are two categories of side-effects of radiotherapy to be considered: First, nausea, vomiting, and malaise after treatment and, second, leukopenia and depression of platelets and eventual anemia. In the first category, derivatives of vitamin B complex, such as nicotinamide or nicotinic acid, with or without pyridoxine hydrochloride, have been helpful on clinical trial. Gravidox, which is a mixture of 20 mg. of pyridoxine hydrochloride and 20 mg. of thiamine hydrochloride, three tablets three times a day, may be helpful. In regard to the second category, leukopenia and depression of platelets may follow total body irradiation or treatment over large areas of the body as commonly given for lymphomas and leukemias. There is no reason for routine administration of liver extract and vitamin B_{12} for this difficulty. Small doses of cortisone acetate, usually 25 mg. given twice daily, until the white blood cell count returns to normal, may be helpful in many cases. Many experiments with animals have been reported using glutathione and cysteine after heavy doses of total body irradiation, but it is not believed that these substances have been used to any extent clinically.

POSTNASAL TAMPON FOR NASAL HEMORRHAGE

To the Editor:—*Is there information available on the origin of the routine postnasal pack used for nasal hemorrhage?*

Ernest E. Alein, M.D., San Francisco.

Answer.—A brief mention of the postnasal tampon technique was given by Philipp Scheck in 1884. The historical documentation of this procedure is not so simple, as it means ferreting out of a case description of such a technique that might be so identified. Priority is lost in antiquity and may not be well established, but one of the best descriptions was offered by P. McBride in his "Diseases of the Throat, Nose and Ear" (ed. 2, Philadelphia, P. Blakiston's Son and Company, 1894, pp. 272 and 273). It follows: "If it is desired to plug the posterior nares a small-sized, soft rubber catheter is the best instrument to employ. To its extremity is attached a string of sufficient length. The point is now passed into the nostril, while the patient sits, with open mouth and light thrown on the pharynx, before the surgeon. When the latter sees the catheter appear below the palate he seizes it with dressing forceps, and pulls it and the attached string out through the mouth. A pledget of lint, preferably saturated with vaseline, to which some antiseptic has been added, if there be a prospect of the plug having to remain *in situ* for any length of time—is now attached to the string about 18 inches from its extremity, and pulled up behind the palate, after which the two projecting strings are tied together. It is often useful at this juncture, to introduce the finger to guide the pledget past the uvula and soft palate. If it be only desired to plug the anterior nares, a long strip of lint—saturated with vaseline to prevent sticking—is pushed in by dressing forceps. Plugs produced by distending membranous or india rubber bags, with air or fluid, have been employed, but they seem only complicated methods of arriving at the same result."

INSECTICIDAL FOGGING OF HOSPITAL GROUNDS

To the Editor:—*We purchased an insecticidal fogging machine in an endeavor to control mosquitoes and flies in the vicinity of the hospital grounds. The active ingredients in the insecticide used are chlorophenothane, 8%; isobornyl thiocyanoacetate, 1.55%; related terpenes, 0.45%; and petroleum distillate, 92.5%. Please advise as to the danger, if any, to human and plant life and, also, as to the precautions to be taken and/or substitutes to be used in the fogging procedure to rid the area of mosquitoes and flies.*

Louis J. Ptacek, M.D., Oconomowoc, Wis.

Answer.—If the fogging is done by responsible and trained persons acquainted with the dispersal of such preparations, it is rather unlikely that members of the hospital community would be exposed to dangerous amounts of the material from either acute or chronic toxicity viewpoints. Contamination of fruit or vegetables in gardens or in the hospital is equally unlikely because of the nature of the dispersal and the small quantities of the insecticidal materials used. Persons suffering from asthma or hay fever might experience respiratory difficulty if they were in immediate contact with the fog. Fogging operations, however, are usually conducted after sundown, or later in the evening, and at distances of 25 to 50 ft. from the nearest dwellings. The nature of the dispersal and the meteorologic conditions for successful fogging operations are such that gross exposure to fogs by such persons can be readily avoided. Wildlife is reported to be not injured when large areas of forest are fogged with chlorophenothane. Birds, bees, butterflies, and other forms of beneficial life commonly seen around residential areas are also probably safe for the same reasons.

TREATMENT OF HYPERPIGMENTATION

To the Editor:—*I would like information regarding the use of monobenzyl ether of hydroquinone in the treatment of hyperpigmentation of the skin.*

E. G. Kettelkamp, M.D., Monona, Iowa.

Answer.—Monobenzyl ether of hydroquinone (MBH) is the only known chemical agent that inhibits the formation of melanin pigment when applied to the skin. Other drugs, including the so-called bleach creams, bring about an apparent decrease in skin pigmentation by exfoliation of the outer pigmented horney layer. Although MBH is an effective topical agent for decreasing melanin pigmentation, it has several major disadvantages: 1. About 13% of patients develop a contact dermatitis. 2. The decrease in pigmentation is very slow, requiring six to nine months in some patients. 3. The resulting depigmentation is often not uniform but mottled, especially in the Oriental and Negroid races. 4. For some unknown reason MBH is effective in only a relatively small percentage of patients treated. The use of MBH should therefore be limited to disfiguring melanin hyperpigmentation in the Caucasian race. If no effect is noted after 9 to 12 months of application, therapy should be discontinued. MBH, being an inhibitor of melanin formation, has no effect on pigmentation resulting from iron, silver, or artificial pigments. A commercially available ointment contains 20% MBH in a washable base.

FISH POISONING

To the Editor:—*A patient in Havana, Cuba, had an acute episode of diarrhea lasting seven days. He claimed to have eaten fresh broiled barracuda meat, which he caught himself. Even though the barracuda is a man-eating fish, is there any special reason why this type of fish poisoning is different from other fish or shellfish poisoning?*

C. D. J. Generales, M.D., New York.

Answer.—Fish poisoning resulting from the ingestion of fresh (unspoiled) barracuda is generally classed under the syndrome known in the Caribbean area as ciguatera. More than 300 species of fish have been reported as being capable of producing ciguatera-like symptoms. Prolonged diarrhea is a common component of this complex. The only relationship between the barracuda's man-eating tendencies and its toxicity is its size, i. e., only the larger specimens are likely to be dangerous. Shellfish poisoning is caused by a toxic substance found in certain marine protozoa (dinoflagellates), on which the shellfish inadvertently concentrate for food during certain seasons of the year. The poisonous substance that produces shellfish intoxication is not the same as that which produces ciguatera-like symptoms.

BCG VACCINATION

To the Editor:—*May I point out in answer to the query entitled "Exposure of Children to Tuberculous Grandmother" (J. A. M. A. 161:926 [June 30] 1956) that I would recommend BCG vaccination if the grandchildren have a negative reaction to the tuberculin test. Six to eight weeks after vaccination, if the children's reactions to the tuberculin test have become positive, let them visit the grandmother, who I assume is receiving antimicrobial treatment. I would have the grandmother as well as the children take the accepted precautions against infectious disease. This advice is based on my long experience, both in the laboratory and in the field, with the use of attenuated, viable tubercle bacilli as immunizing agents against tuberculosis and is supported by the experiences of other investigators. The consultant's answer has become practically a slogan for those who have had little experience with immunizing agents in tuberculosis and has also been used by opponents of other forms of vaccination and treatment. It would be of interest to readers of* The Journal, *and to those of us engaged in the study of immunization against tuberculosis, if the consultant would present the statistical data on which he bases his statements and compare them with the data of Ferguson, Rosenthal, the Medical Research Council, myself, and others who have evaluated BCG vaccine under control conditions.*

In support of my own views, may I summarize a study, which was initiated in 1936 and which culminated in 1956, to determine under field conditions the value of BCG vaccine. A group of 1,551 children of preschool and school age who had negative reactions to the tuberculin test received an intracutaneous injection of BCG vaccine and were not revaccinated. A group of 1,457 children of comparable age and sex who had negative reactions to the tuberculin test received an intracutaneous injection of saline solution and served as controls. An analysis of 28,580 roentgenograms of the chest taken annually for the first 9 to 11 years of this study showed that 4.1% of the vaccinated and 16.4% of the control patients showed

tuberculous lesions—0.7% miliary in nature, none among the vaccinated; 12.5% and 14.8% of the vaccinated and control patients, respectively, showed nontuberculous lesions. An appraisal of the protective value of BCG vaccine, 15 years after the initiation of the same study, was published in THE JOURNAL *(149:334 [May 24] 1952) by C. F. Aronson and me. At that time, 12 of the vaccinated and 65 of the control patients had died of tuberculosis while 59 and 63 of the vaccinated and control patients, respectively, had died from nontuberculous causes. Of the 65 deaths from tuberculosis, 19 had been due to miliary tuberculosis. None of the vaccinated patients had died from this form of tuberculosis.*

In 1956, 18 to 20 years after the initiation of the study, we again determined the mortality from all causes and from tuberculosis among the 3,007 persons in the study, and traced all but 24 persons. At this time we found that 13 of the vaccinated and 68 of the control patients had died from tuberculosis, 45 of the vaccinated and 42 of the control patients had died from nontuberculous diseases, and 44 of the vaccinated and 40 of the control patients had died from the results of violence.

The preliminary report of the Medical Research Council, published in the British Medical Journal, *Feb. 25, 1956, shows that among over 50,000 adolescents followed in this study the annual incidence of tuberculosis was 0.37 per 1,000, compared with 1.94 per 1,000 among the control patients. Will the consultant cite any reference indicating that multiple cases of tuberculosis have followed the use of BCG vaccine from one laboratory or from one lot of vaccine?*

Joseph D. Aronson, M.D.
Henry Phipps Institute
Philadelphia.

For additional discussion of this subject, see THE JOURNAL, Oct. 13, 1956, pages 698-700.—ED.

RESEARCH REVIEWS

From time to time there will be published in this section of THE JOURNAL *brief but not necessarily complete reviews of some of the newer clinical aspects of medical research and practice. This material is gathered specifically for* THE JOURNAL.—ED.

NONSPECIFIC DEFENSE MECHANISMS OF THE BODY

Current interest in the study of natural resistance to infection found expression at a conference of the New York Academy of Sciences, Section of Biology, in New York. The mechanisms of "general resistance" are being unraveled gradually. There are several independent defense systems by which the body guards against invading bacteria, viruses, and protozoa. Some of these mechanisms have been defined recently.

The Properdin System.—The recognized components of the properdin system are properdin, complement, and magnesium ions.[1] According to its discoverer, L. Pillemer,[2] Western Reserve University, Cleveland, properdin is a euglobulin that contains lipid, carbohydrate, and phosphorus. It is normally always present in the serum of man and mammals without previous antigenic stimulation. Serum from rats reared under sterile conditions contains a normal amount of properdin. Properdin is not an antibody. Its action is nonspecific. To become active, properdin requires complement (C′) and magnesium ions.

While it was thought in the past that the presence of antibody is necessary for the action of complement, the discovery of the properdin system has demonstrated that complement also plays a part in bactericidal defense mechanisms that act in the absence of specific antibodies. Four components of complement have been identified: C′1, C′2, C′3, and C′4. All four components are essential in the properdin system. To kill gram-negative bacteria, for instance, C′1, C′2, C′3, C′4 and magnesium ions must be present.

Magnesium in the properdin system cannot be replaced by sodium or calcium. Under experimental conditions—and only in unphysiologically high concentrations—cobalt or manganese may replace magnesium. Thus, under normal circumstances, magnesium plays an essential part in the body's natural defense against infection.

Normal human serum contains 4-8 units of properdin per milliliter, rat and mouse serum 25-50 units, and guinea pig serum less than 3 units. One may speculate whether these species variations reflect differences in natural resistance to infection. Stray dogs have a properdin level that varies from the normal for dogs of 12 to 18 units per milliliter to near 0. In some areas, especially in the South, stray dogs have an almost uniformly low titer. If they are given proper care and good food, their titer can be restored to a normal level.

In normal individuals the properdin level remains constant. It bears no relation to age or sex. L. Pillemer [2] and C. F. Hinz Jr. and J. R. Murphy,[4] Western Reserve University, Cleveland, have reported that fever, variations in the leukocyte count, and some other factors do not influence the properdin level. In patients with infections due to gram-negative bacteria, pneumococci pneumonia, and paroxysmal nocturnal hemoglobinuria, it has been found that the properdin level is low.

In vitro, the properdin system present in normal human serum destroys bacteria, inactivates viruses, kills protozoa, and lyses abnormal erythrocytes. In experimental animals, there appears to be a relation between the serum properdin level and shock, susceptibility to bacterial invasion after irradiation, and resistance to infection in general.

J. Fine, Harvard Medical School, Boston, and his collaborators have found that hemorrhagic shock in dogs reduces the serum properdin level considerably, while there is no change in the total and differential leukocyte count or in the hemolytic activity of complement in vitro.[5]

O. A. Ross,[6] Western Reserve University, Cleveland, has reported that total body irradiation of mice results in a profound drop in the properdin level and fatal bacteremia. The effects of the administration of properdin under these circumstances have been studied. When properdin is given during the postirradiation period, it partially protects the animals and prevents death. When it is given too early, it does not prevent the onset of bacteremia. Pillemer believes that it may be dangerous to give properdin at the height of bacteremia, since its bactericidal action may release such an overwhelming amount of endotoxin at one time as to cause toxic shock and death.

The bactericidal action of the properdin system has been demonstrated.[7] When bacteria invade the blood stream they are attacked immediately. This is a nonspecific effect. Specific antibodies in response to antigen stimulation are only formed after several days. The properdin system thus forms the first defense. Its action is supplemented by the formation of antibodies that deal with the surviving bacteria.

According to D. Rowley,* St. Mary's Hospital, London, England, the lipopolysaccharide fraction in bacterial cell walls may be the substrate for the serum bactericidal reaction. He found that following the injection of cell walls of various gram-negative bacteria there were changes in nonspecific immunity to experimental infection with Escherichia coli and Salmonella typhosa. In addition to these organisms, M. Landy,* Army Medical Service Graduate School, Washington, D. C., has shown that injection of lipopolysaccharides into mice also causes a transient increase in nonspecific resistance to experimental infection with Proteus vulgaris and Pseudomonas aeruginosa. This increase in resistance following bacterial lipopolysaccharide injection is accompanied by elevated properdin titers.[10]

Highly purified lipopolysaccharides have been prepared.[11] Lipopolysaccharide from Salmonella abortivoequina is a powerful pyrogen, and its effects when injected into man have been studied.[12] The question yet to be answered is whether injection of such lipopolysaccharides prepared commercially offers a practical way of raising the properdin level clinically.

Fresh normal serum inactivates influenza A and B, mumps, Newcastle disease, and vaccinia viruses; in conjunction with antibody, it also inactivates Rous sarcoma, Western equine encephalomyelitis, herpes simplex, and dengue viruses. It is inactive against poliomyelitis and the recently described adenoviruses. H. S. Ginsberg and R. J. Wedgwood,[13] Western Reserve University, Cleveland, have shown that the properdin system inactivates the virus of Newcastle disease. There is no evidence yet as to the role that the properdin system may play in natural or acquired immunity to viral infection in man. The heat-labile component of normal serum reported in 1949, which neutralizes virus infectivity and inhibits hemagglutination,[14] is probably identical with properdin.[1]

Also, the heat-labile serum components and magnesium required for toxoplasma antibody to exert its adverse effect upon the parasite may be identical with the properdin system, according to H. A. Feldman,[15] State University of New York, Syracuse, and other workers.[16]

Recent studies in man [17] indicate that various types of anesthesia, elective surgery, accidental trauma, adrenalectomy, and removal of the spleen do not cause significant changes in the serum properdin titer. The properdin level has been found to be depressed in certain surgical cases in association with peritonitis, pneumonitis, atelectasis, paralytic ileus, gastrointestinal hemorrhage, and wound infection following burns. In a few patients subjected to extreme variations in corticosteroid maintenance therapy after adrenalectomy, no significant changes in serum properdin titer were noted.

At present, properdin is not available for clinical use. Two ways of increasing the amount of naturally occurring properdin are being considered: (1) the injection of lipopolysaccharides and (2) the fractionation of plasma.

Little is known yet about the practicability of the first method. The second method is under intensive study in Boston. Since the preparation of properdin from serum presents a number of difficulties, plasma from blood collected over an exchange resin is being used. Initial laboratory production promises a yield of about 1 million units of purified properdin per year. With pilot plant production, it should be possible to increase this yield to about 6 million units per year, and with other measures now contemplated perhaps to more.

Before properdin can be made available for clinical use, problems of sterility, stability, and freedom from pyrogenic and other untoward effects must be solved. J. Fine estimates that an adult depleted of properdin may require a therapeutic dose of as much as 10,000 to 20,000 units; hence the amount for clinical investigation that may be expected for the time being will be very little indeed.

Other Defense Mechanisms.—J. L. Tullis and D. M. Surgenor,[18] Harvard Medical School, Boston, have reported the isolation of two new proteins that control the ability of leukocytes to ingest bacteria. They were isolated from plasma. One is a betaglobulin; the other, an alpha-1 globulin. They are different in their chemical behavior, but similar in their physiological activity of promoting phagocytosis. They have been called phagocytosis-promotion factors. Purified preparations of properdin have no phagocyte-stimulating effect.

J. G. Hirsch,[19] the Rockefeller Institute for Medical Research, New York, has investigated the mechanism that leads to intracellular death of engulfed micro-organisms. He believes that lysozyme present in polymorphonuclear leukocytes does not account for the bactericidal power of these cells, since many micro-organisms insusceptible to lysozyme are killed in phagocytic cytoplasm. He has isolated a specific protein from the cytoplasm of polymorphonuclear leukocytes, which is thought to be responsible for the bactericidal action. The name phagocytin has been proposed for this protein. Its enzyme type of action is different from that of previously known antibacterial agents derived from tissues.

The study of these and other factors that may play a role in the natural defense mechanisms of the body is being actively pursued.

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